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ORIGINAL CONTRIBUTIONS

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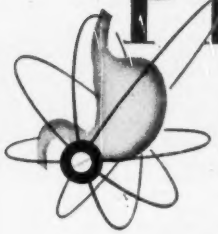

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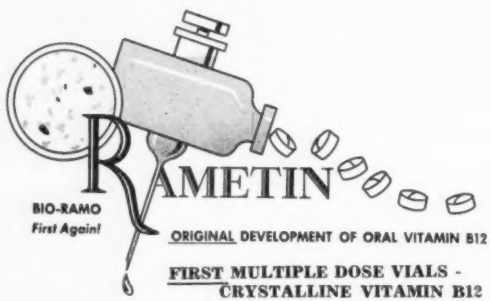

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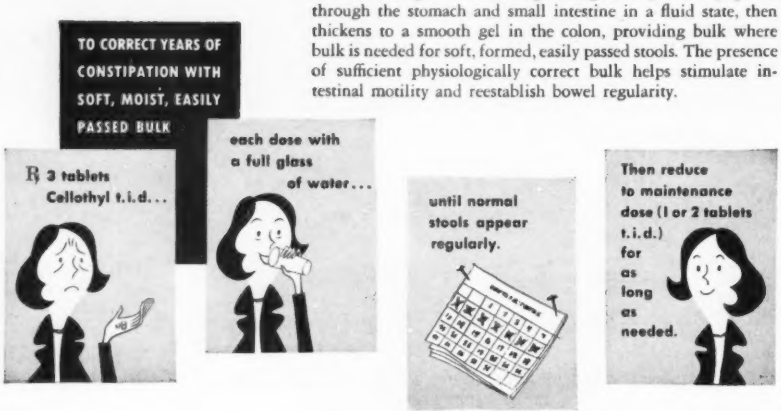
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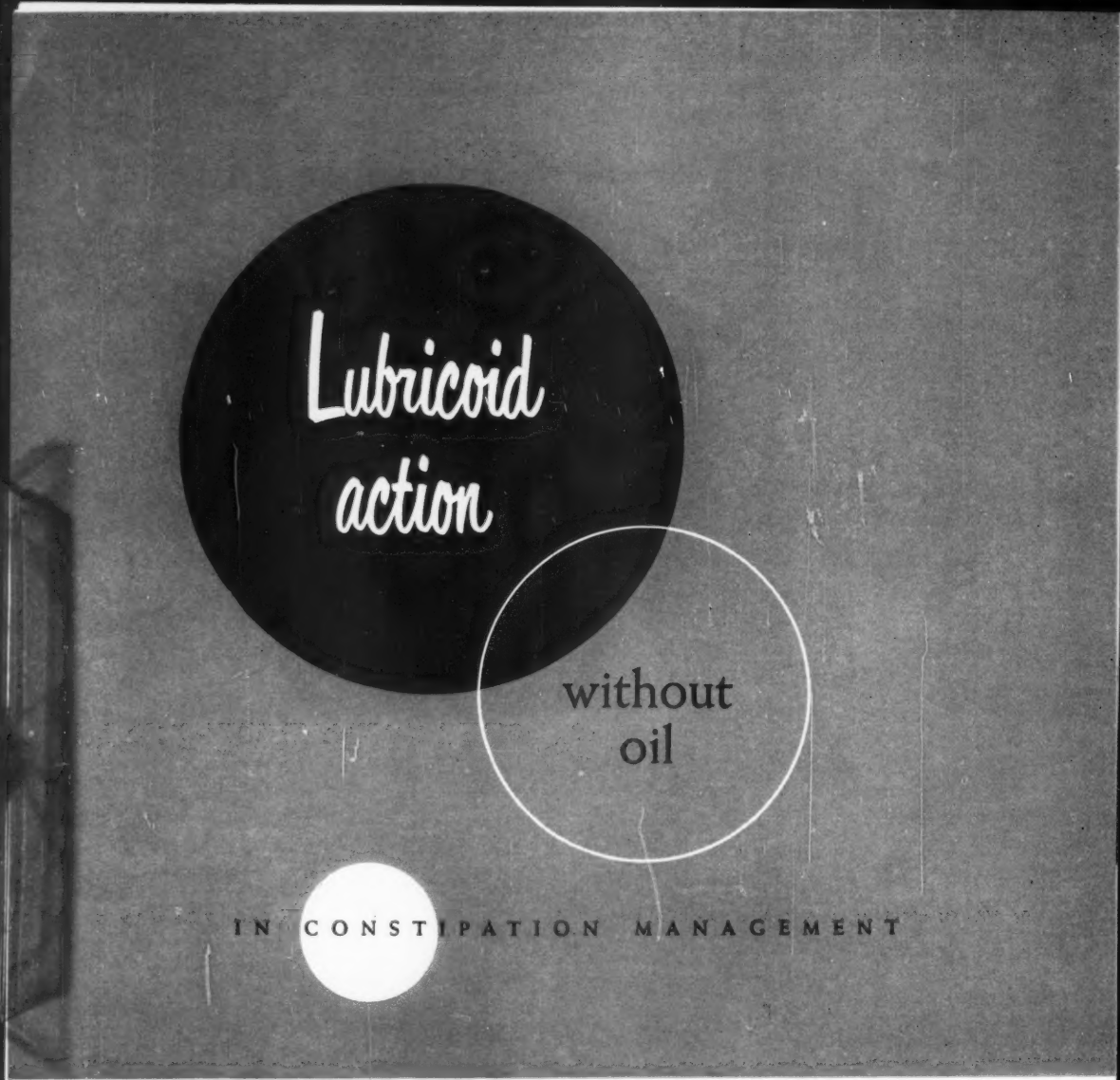

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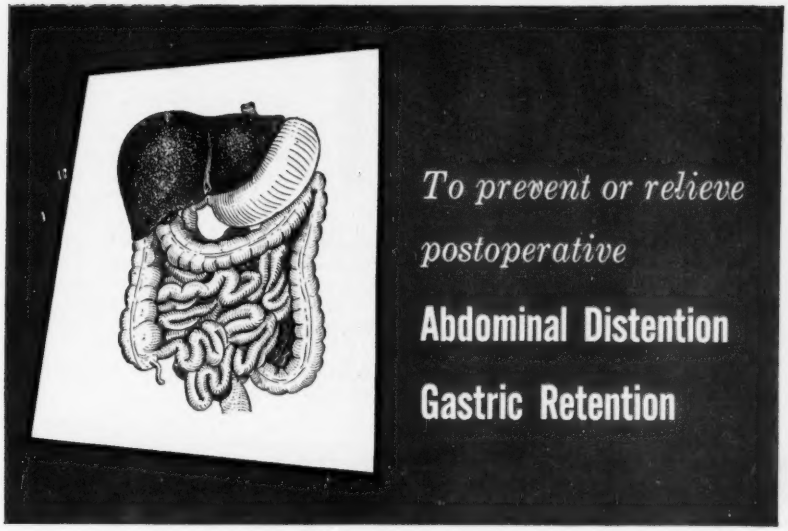

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HYPERINSULINISM — A FACTOR IN RHEUMATOID ARTHRITIS

E. M. Abrahamson, Ph. D., M. D., New York, N. Y.

DIABETES MELLITUS (hypoinsulinism) is only rarely accompanied by asthma (1), peptic ulcer (2) and rheumatic fever (3). This has suggested the hypothesis that these latter conditions are related to the physiological opposite of diabetes—hyperinsulinism (4, 5, 6, 7). The same line of reasoning has shown hyperinsulinism to be an endocrine or metabolic factor underlying the constitution of the "neurotic" (8).

The recent dramatic cures, or rather symptomatic relief, of rheumatoid arthritis by ACTH (9) and by cortisone (10) have awakened a great deal of interest in that disease. Unfortunately, the drugs are very scarce and costly and many painfully crippled victims of rheumatoid arthritis are clamoring for the relief that is beyond their grasp. These drugs are not entirely innocuous for their use has produced diabetes in some persons to whom they were administered (11). They have also induced symptoms akin to those found in Cushing's disease, such as "moon face" and "buffalo hump" (12). These untoward side reactions are due to the fact that it had not been established that the patients actually lacked the adrenal hormones and the administration of cortisone produced the same excess as is found in hyperadrenalism. ACTH has this effect by stimulating the patient's own adrenal glands to become overactive (13). Good practice dictates initial hospitalization of patients under treatment with either drug so that the proper dosage may be determined under conditions that permit close watch lest disastrous effects of overdosage occur. Furthermore, they must be given indefinitely for their withdrawal is often followed by a return of symptoms, usually much more severe than before the treatment was begun (14). They should not be used to treat persons with hypertension for they sometimes induce dangerously high blood pressures (15). They occasionally cause psychotic episodes (16). They might also mask latent infections, such as tuberculosis, because they tend to diminish febrile reactions (17). On the credit side of the ledger we may cite their successful use in treating acute rheumatic fever (18) and severe asthma (19).

Although statistics as to the concomitant occurrence of rheumatoid arthritis and diabetes are not available, there is the general impression that it is quite rare. In an experience of two decades in two busy diabetes clinics, the author fails to recall a single case of rheumatoid arthritis. On the other hand, hypertrophic arthritis, which is, in a sense, opposite to rheumatoid (atrophic) arthritis, is fairly common among diabetics, especially the elderly ones. Per contra, rheumatoid arthritis usually attacks young adults whom it continues to afflict throughout their lives. Dr. Reginald Burbank, who has treated many thousands of arthritics, has found diabetes in only six of them (20).

There is a constitutional habitus generally associated with rheumatoid arthritis. The patients are usually of the asthenic type (21). This same constitution is found among persons afflicted with allergies, rheumatic fever and peptic ulcer. As was mentioned above, these ailments have been found to be associated with hyperinsulinism. On the other hand diabetes and biliary disease are usually found in the opposite, sthenic, type. It has been noticed that rheumatoid arthritics often become symptom free if they happen to become jaundiced (22).

During pregnancy, there is a tendency toward elevation of the blood sugar level (lowered tolerance) (23). Many female arthritics have had considerable amelioration of their symptoms during gestation (24).

A low carbohydrate diet for rheumatoid arthritis has been in vogue for many years (25). This was based on the finding of rather elevated hyperglycemic responses in applying the standard two hour glucose tolerance test (26). It was assumed that the test indicated impaired glucose tolerance (but not enough to warrant the diagnosis of diabetes). However, it has since been demonstrated that lowered carbohydrate tolerance (diabetes) is best treated by restriction of fats (27, 28) and that curtailment of carbohydrate intake is indicated in hyperinsulinism (28). The dietary treatment that has been recommended has been of some help—but not for the reasons advanced. Furthermore, blanket restriction of carbohydrates, as we shall see presently, does not cover the situation completely.

All of these considerations lead to the possibility that rheumatoid arthritis might be accompanied by hyperinsulinism. If there be any merit to this hypothesis, it must be supported, not by a statistical trend, but by a complete correspondence. EVERY case must indicate, by the six hour glucose tolerance test of Harris (29), that the arthritic has hyperinsulinism as well. The rare cases of simultaneous rheumatoid arthritis and diabetes must have dysinsulinism (30). In this condition, the glucose tolerance test shows the usual diabetic response during the first two or three hours after the ingestion of the glucose and this initial period of hyperglycemia is followed by a profound drop into the hypoglycemic range. Harris believes that this rare metabolic disorder is due to a time lag in the production of insulin followed by an inordinately large secretion of the hormone. A single failure to obtain hypoglycemia in subjecting rheumatoid arthritics to the glucose tolerance test would completely demolish the theory.

This hypothesis was tested in five patients. Fortunately, the first case had diabetes as well as rheumatoid arthritis, the latter diagnosis having been made at one of New York City's leading hospitals. The six hour glucose tolerance test fulfills all the criteria for dysinsulinism (Curve A). The small figures over the segments of the graph indicate the grams of glucose excreted during the corresponding intervals. If the curve had been plotted for but two or three hours, it would have been unquestionably called a diabetic curve. However, the subsequent drop into the hypoglycemic range makes it indicative of dysinsulinism. The patient left New York City, making further observation impossible.

The second case was that of a woman of 56 who had had "rheumatism" since her early thirties. Her hands had the typical appearance of moderate rheumatoid arthritis. She had had repeated episodes of pain

Adjunct Attending Physician, The Jewish Hospital of Brooklyn.

Submitted June 29, 1951.

and limitation of motion in all her extremities. In November, 1950, she had an attack of severe pain in the middle of her neck. Her hands and feet also became much more uncomfortable than usual. Her temperature fluctuated between 99 and 100.8°. Her sedimentation rate was 48 mm in an hour. The trapezii muscles were spastic and tender. Otherwise, the only positive physical sign was tenderness in the left upper abdominal quadrant. With deeper pressure, there was some protective spasm of the left rectus abdominalis. These findings have been shown by Harris to be found with hyperinsulinism (29). The tenderness and spasm are probably due to sensitivity of the tail of the pancreas where the islands of Langerhans are concentrated.

She was prescribed tablets of Empirin Compound with ½ grain of Codeine every four hours. She was massaged and her neck was supported by a "Foam Cloud Pillow" which is a small pillow about the size and shape of a loaf of bread. One side has a concavity into which the neck fits as the patient lies on it.

As soon as the temperature remained below 99.6° and her pain became bearable without medication, she was subjected to the six hour glucose tolerance test. The results are indicated by Graph B. Her serum calcium was 8.8 mgs per 100 cc. This tends to be somewhat low in hyperinsulinism (31).

These findings demonstrate that this patient, who had just partially recovered from an acute exacerbation of rheumatoid arthritis, also had hyperinsulinism. If one wishes to restore the beam of an unequally loaded balance to the horizontal position, one can either increase the lighter weight or diminish the heavier. By the same token, we should be able to accomplish at least some amelioration of symptoms by diminishing the output of insulin as well as we can by increasing the flow of the antagonistic adrenal hormone, either by stimulating the adrenal cortex with ACTH or by supplying exogenous cortisone. The patient was therefore prescribed Harris's diet (modified slightly to conform with local dietary customs) to suppress the hyperinsulinism (28). She was advised to continue her habit of taking aspirin whenever her discomfort required it.

This diet is based on four principles. It is relatively high in fat which depresses the activity of the insulin apparatus (27, 28, 32, 33, 34). Carbohydrates are restricted to those slowly digested and absorbed in order to avoid stimulation of the islands of Langerhans by any marked rise in blood sugar (35). The food is taken in frequent small meals to prevent any large rise in blood sugar and to compensate for any postprandial fall in blood glucose. Caffeine is absolutely interdicted because it is a common exciting cause for hyperinsulinism (28). It induces glycogenolysis, causing the rapid rise in blood sugar we wish to avoid (36).

ON ARISING—Medium orange, half grapefruit or 4 ounces of juice.

BREAKFAST—Fruit or 4 ounces of juice; one egg with or without 2 slices of ham of bacon; *only one* slice of bread or toast with plenty of butter; beverage.

2 HOURS AFTER BREAKFAST—4 ounces of juice.

LUNCH—Meat, fish, cheese or eggs; salad (large serving of lettuce, tomato or Waldorf salad with mayonnaise or French dressing); *only one* slice of bread or toast with plenty of butter; dessert; beverage.

3 HOURS AFTER LUNCH—Glass of milk.

1 HOUR BEFORE DINNER—4 ounces of juice.

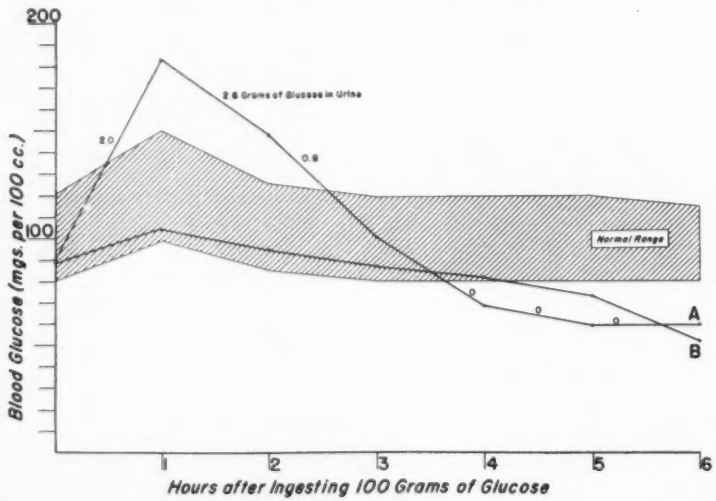
DINNER—Soup, if desired (not thickened with flour); vegetables; liberal portion of meat, fish or poultry; *only one* slice of bread or toast, if desired; dessert; beverage.

2-3 HOURS AFTER DINNER—Glass of milk.

EVERY 2 HOURS UNTIL BEDTIME—4 ounces of juice, fruit or a few nuts.

ALLOWABLE VEGETABLES—Asparagus, avocado, beets, broccoli, Brussel sprouts, cabbage, cauliflower, carrots, celery, corn, cucumber, egg plant, lima beans, onions, peas, radishes, sauerkraut, squash, stringbeans, tomatoes, turnips.

ALLOWABLE FRUITS—Apples, apricots, berries, grapefruit, melons, oranges, peaches, pears, pineapple, tangerines. These may be cooked or raw, with or without cream but without sugar. Canned fruits should be those packed in water (not syrup).



JUICE—Any *unsweetened* fruit or vegetable juice except grape juice or prune juice.

BEVERAGES—Weak tea (tea ball, not brewed), Postum, decaffeinated coffee.

DESSERTS—Fruit, unsweetened gelatine, junket (made from tablets, not the mix).

ALCOHOLIC AND SOFT DRINKS—Club soda, dry ginger ale, distilled liquors.

SUNDRIES—Lettuce, mushrooms and nuts may be taken as freely as desired.

AVOID ABSOLUTELY—Sugar, candy and other sweets, cake, pie, pastries, custards, puddings, ice cream. Potatoes, rice, grapes, raisins, plums, figs, dates, bananas. Spaghetti, macaroni, noodles. Wines, cordials, cocktails, beer. Caffeine (ordinary coffee, strong brewed tea, caffeinated soft drinks).

This diet is very efficacious in raising the general level of the blood sugar. However, personal experience has demonstrated in many cases that administration of calcium salts hastens the cure (8, 37). The preparation used was "Calphosan" (R) of which 10 cc were injected intragluteally once a week for a month. This suffices to raise and maintain the serum calcium level (37). It is felt that raising the serum calcium artificially makes the body's adjustment easier since the serum calcium level more or less parallels that of the blood glucose (31). At any rate, in past treatment of very many cases of hyperinsulinism, the length of treatment was materially shortened by administering the calcium salt along with the diet.

After she had been on the diet for six weeks, the left rectus spasm and left upper quadrant tenderness were no longer elicited. This has been found to be a satisfactory criterion of metabolic adjustment (8). Repetition of the glucose tolerance test is to be avoided because the sudden and, by now, unaccustomed overloading of the insulin apparatus might reestablish the original symptoms (8). In the mean time, the patient found that she no longer required any aspirin. Her pains had all but disappeared. The "knots" could no longer be felt in her muscles. There was, of course, no visible change in her joints.

The rigid dietary regime was relaxed somewhat. Carbohydrates were permitted in more liberal quantities and the frequency of feedings was reduced.

BREAKFAST—Fruit or juice; cereal (dry or cooked) with milk or cream and/or one or two eggs with or without two slices of ham or bacon; *only one* slice of bread or toast with plenty of butter; beverage.

Lunch—Meat, fish, cheese or eggs; salad (large serving of lettuce, tomato or Waldorf salad with mayonnaise or French dressing); *only one* slice of bread or toast with plenty of butter; dessert; beverage.

MID-AFTERNOON—Glass of milk.

DINNER—Soup, if desired, (not thickened with flour); vegetables; liberal portion of meat, fish or poultry; *only one* slice of bread or toast, if desired; dessert; beverage.

BEFORE RETIRING—Snack consisting of milk, crackers and cheese, half sandwich or fruit.

All vegetables and fruits are permitted.
The other restrictions were not changed.

After a month, she was found to be very comfortable and a further modification was possible. She was permitted a sweet dessert only with dinner. However, her sweet tooth had been painlessly extracted and she rarely took advantage of this permission.

After another month, she was still free from pain. The tenderness and spasm in her left upper abdominal quadrant had not returned. She was then permitted to abandon the diet except for three restrictions—1. She avoided all caffeine beverages. 2. She was moderate in her consumption of sweets. 3. She always ate something before retiring.

Except for an occasional ache during the exceptionally humid month of May, 1951, which yielded very promptly to a small dose of aspirin, she has been free from any significant discomfort. Her sedimentation rate (on June 20, 1951) was 22 mm in an hour (practically normal). She has no fatigue, for the first time in twenty years. Her joints have not changed in appearance but they are much more mobile. The muscles are normally supple and they are entirely free from "knots."

Three other patients with rheumatoid arthritis were investigated in the same fashion. The laboratory findings were qualitatively identical with this case. The same treatment was instituted but the patients have not been under observation long enough to draw any conclusions.

DISCUSSION

One naturally hesitates to draw sweeping generalizations from but one well observed case (not counting the others). However, it was postulated that the very first case had to have hyperinsulinism or the hypothesis would be completely demolished.

The explanation for the restoration of comfort is not hard to find. This patient had been subjected to a state of chronic partial glucose starvation for many years. With restoration of normal blood glucose levels, the muscles were better nourished and they responded with more normal function. The spasms were relieved and this produced less pressure on the sore articular surfaces and less strain in the muscles, themselves. That is sufficient to relieve the pain and to permit greater motion in the joints.

All of these patients were ambulatory and were therefore only mildly afflicted with rheumatoid arthritis. It is admittedly questionable whether we would have the same therapeutic success with the severer types of rheumatoid arthritis. Yet there is some justification for presenting this single case. Its publication will permit others to test this theory promptly. Aside from its theoretical interest in demonstrating again the antagonistic actions of insulin and cortisone, it might lead to a sound therapy even for severe cases of rheumatoid arthritis. One could treat these cases initially with either ACTH or cortisone. Once the acute symptoms had been corrected, the patients could be switched to the dietary treatment to maintain comfort without subjecting them to the well recognized dangers of excessive or too prolonged use of the powerful hormones. It would enable many more crippled victims of rheumatoid arthritis to obtain relief for there isn't enough of either drug to satisfy the enormous demand. But all this is highly speculative. We must await the results of a thorough test.

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THE EFFECT OF BANTHINE ON THE GASTRIC SECRETION OF YOUNG, NORMAL SUBJECTS

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THIS STUDY WAS undertaken with the object of determining the effect of therapeutic doses of Banthine on the gastric acidity and on the volume secretion in young, apparently healthy subjects.

Fifty first year medical students volunteered as subjects for this test. During the course of this investigation, the number was reduced to thirty-two. The ages of the students varied from 21 to 27.

METHOD

Each student submitted to gastric intubation on two mornings, a week apart in 29 cases, and three weeks or longer in 3 cases. The day before each test, half of the subjects received two capsules, each containing 50 mg. Banthine; the other half received similar-appearing capsules containing lactose, and vice versa. One capsule was taken on retiring, the second, half-an-hour prior to the passing of a Levine tube. The fasting stomach was emptied and the quantity of secretion recorded. The test meal consisted of four arrowroot biscuits and twelve ounces of water. Samples were withdrawn 30 and 90 mins. after the meal, on the second occasion the stomach being evacuated as completely as possible, and the total quantity recorded. The individual samples were titrated for free and total acidity, using Topffer's and phenolphthalein as indicators.

From the Jewish General Hospital, Montreal, Canada.
Submitted July 12, 1951.

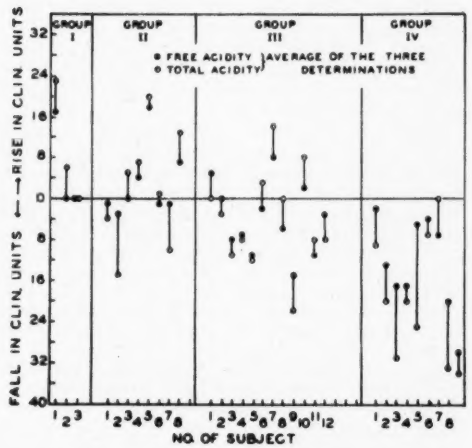
RESULTS

The free acidity increased in 7 of the subjects; remained unchanged in 4; and decreased in 21. A more

detailed study of the data revealed that most of the cases in which a rise occurred had a low acidity or achlorhydria in the control test. The subjects were therefore divided into four groups according to the amount of free Hcl present in the control test. The average of the three determinations was taken as the basis of classification and comparison: group 1 consisting of subjects with achlorhydria; group 2 of those with a range of free Hcl up to and including 19 clinical units; group 3 from 20 to 39; group 4 from 40 up. The results were charted on the basis of the degree of rise or fall of both free and total acidity in each of the four groups. It will be seen (Chart 1) that in group 2 a slight fall occurs in four of the subjects; in group 3 the fall is more pronounced and occurs in a greater proportion of the subjects; in group 4 the effect is still more pronounced.

CHART 1

EFFECT OF BANTHINE ON FREE AND TOTAL ACIDITY OF HEALTHY YOUNG SUBJECTS



The black dot indicates the free Hcl; the circle, the total acidity. The position of the dot and circle above or below the 0 line indicates, in clinical units, the rise or fall in acidity under the influence of 100 mg. Banthine given in two doses, 9 hours apart.

The significance of the original acidity in relation to the effect of Banthine is shown in Table 1.

TABLE 1.

CONTROL			BANTHINE		
GROUP NO.	NUMBER OF SUBJECTS	FREE HCL IN CLIN UNITS	NO. SUBJ. WITH FREE HCL FALL	%	AVERAGE FALL IN CLIN. UNITS
1	3	ACHLORHYDRIA	0	0	0
2	8	1 TO 19	4	50	UNDER 2
3	12	20 TO 39	8	66·6	8
4	9	40 AND OVER	9	100	12·8
ALL GROUPS	32		21	65·6	5·7

A comparison of the figures obtained for the entire group of 32 subjects with the group of 9 showing the highest levels of free Hcl in the control studies, is very illuminating. A fall in the free Hcl occurred in 21 subjects (65.6%) with an average fall of 5.7 clinical units in the former, while in the latter a fall occurred in 100% of the subjects and the average fall was 12.8 clinical units.

The effect of Banthine on the volume secretion was not evaluated. While an effort was made to empty the stomach completely in each final evacuation, we were not entirely satisfied that this was accomplished in all subjects, and we therefore did not attempt to analyze our figures.

None of the subjects complained of any untoward effects. With the doses employed, there was no significant effect on the blood pressure (it fell slightly, rose slightly or remained unchanged), the variations found in this group of subjects being within the limits of normal fluctuation.

Summary and Conclusions

1. The effect of Banthine on the gastric secretion was studied in a group of 32 normal subjects whose ages ranged from 21 to 27, following the administration of one 50mg. tablet about 9 hours, and a second tablet 30 mins. prior to the test meal.

2. While 65.6% of the entire goup showed a fall in the free Hcl values, the average fall in clinical units was only 5.7. When broken down into four groups on the basis of the free Hcl level of the control test meal, two of the groups showed a more pronounced fall. In group 3, with acidity values ranging from 20 to 39, 66.6% showed a fall, the average being 8 clinical units; in group 4 a fall occurred in 100% of the subjects, with an average fall of 12.8 clinical units.

3. In the group of subjects studied, the inhibiting effect of Banthine on the secretion of free Hcl appears to bear a relation to the acidity normally present in the individual, the greater the acidity, the greater the fall after Banthine.

4. The percentage of subjects showing a fall in free Hcl values after Banthine is also greater in the groups showing higher control values.

5. Banthine, in the doses employed, did not produce any perceptible change in the blood pressure which could be attributed to the drug.

The author wishes to express his thanks to Dr. C. M. Ballem for his technical assistance and to the Royal Victoria Hospital for facilities in carrying out part of this work; to Professor F. C. MacIntosh and Associate Professor Norris Giblin of the Dept. of Physiology, McGill University, for their aid in obtaining student volunteers.

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A SIMPLIFIED METHOD FOR THE CALCULATION OF DIABETIC DIETS

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A RECENT SURVEY of actual diabetic practice among members of the American Diabetes Association revealed that the majority still aimed for normoglycemia in their patients (1). At the same time, practically all found it unnecessary for their patients to weigh their food in order to attain this goal. Instead they make use of the relatively simple household measure-serving technique with exchange lists. This is the method which has found widespread favor in recent years (2). In fact, even among those few members of the American Diabetes Association who prefer to disregard glycosuria among their patients, 70% use this patient routine also.

By contrast with the normoglycemic aim of treatment of the above group, it has been the author's experience that there has been much apathy toward pursuing vigorous therapy on the part of the general practitioners who see and treat most of the country's diabetics. Too frequently the patients are simply told to eschew free sweets and pastries and to avoid obesity, with or without the addition of insulin as needed.

While a minority of the general practitioners may take this indifferent attitude through conviction, the majority probably do so because of the time consuming methods of food calculations available in the past (3, 4). Yet, the only calculations actually needed to achieve normoglycemia are the total number of grams of carbohydrate, protein, and fat of the patient's diet (1). In an attempt to remove this stumbling block, the author in 1949 decided to devise a system of food calculation which would be simple, accurate, and capable of being readily memorized. This is a report of the development of this new unit system of diet calculation.

All the food values were completely reconsidered as follows: first, the only figures to be used were those of readily available carbohydrate, rather than the theoretical content. The former is a better index of hyperglycemic effect. Second, the values used for carbohydrate content need satisfy only the minimum required constancy of the daily diet rather than the maximum possible accuracy as hitherto.

These revisions were made possible by a number of factors. In the first place, with the use of continuous acting insulin, the slowly produced hyperglycemic effect of protein and fat can be adequately neutralized. Accordingly, one average value of 6 grams for the protein content of an ounce of predominantly protein source food is adequate in spite of the considerable variation present. The same consideration holds for fat source foods.

In the second place, recent work had revised downward our estimates of the carbohydrate content of vegetables important for diabetic metabolism and hyperglycemia. This had been the result of the focusing of attention on the *available* sugar and starch as contrasted with *total* carbohydrate which included materials which were indigestible or carbohydrates not metabolized as glucose (5, 6). Then, further corrections were made for the lesser carbohydrate content of cooked food as compared with fresh (7). Thus, the 5% vegetables turned out to be 1 to 5% and the 10% vegetables 6 to 10%, with averages of 3 and 7% respectively.*

Secondly, a survey of the eating habits of a large group of our own clinic patients showed that they ate at most only 1 or 2 servings daily of the above 3% vegetables.** In view of this finding, one could allow unlimited choice of average portions of these 3% vegetables, yet could assume that these patients would eat about an equal number of portions of 3 as of 7% vegetables. With this in mind, if we calculated the 7% as 10% vegetables, we could then omit the 3% vegetables altogether from the physician's calculations without loss of accuracy. This maneuver was of value in simplifying the vegetable list. The fruit exchange list, based on portions containing 10 gms. of carbohydrate, is still retained as such.

Finally, the usual milk calculations were changed. Milk is usually listed as containing 12 grams of carbohydrate in an eight ounce (240 cc.) glass. There has been much confusion in an extensive literature on the subject of the assimilation of milk sugar, lactose, by normals and diabetics. Recent work in rats, more accurate because of the control of the calcium as a variable and the use of more refined quantitative analysis of galactose, has clarified the problem (10). The galactose half of the lactose has a decreased effect on the blood sugar because of a delay both in the intestinal hydrolysis of the lactose and in the absorption of the galactose, in contrast to the prompt absorption of the glucose half. In these experiments, 1 hour after ingestion only 72% of the available galactose had been assimilated, and after 3 hrs. a total of 88%. Accordingly, for purposes of its effect on the postprandial blood sugar, 80% of the usual 12 grams of carbohydrate or 10 grams, are assigned to the 8 ounce glass of milk.

As a result of the above, the following diet plan was evolved:

The patient serving exchange method is retained in the usual form (2) with the exception of the vegetable list which is now itemized as follows:

CLASS I. Amts. unlimited, except where specified.

Asparagus	Greens	Onions, any
Broccoli, 1 cup	(beet, chard, dandelion, turnip tops)	Radishes
Brussels Sprouts, 10	Green pepper, 1 large	Rhubarb
Cauliflower	Kale, Kohl Rabi	Squash, summer
Celery	Lettuce	Spinach
Cabbage, sauerkraut		Stringbeans
Cucumber, dill pickle		Tomatoes
Egg plant, 1 cup		Turnip, ½ cup

*Further refinements would involve a study of the influence upon the time of assimilation of the variations in speed of digestion. 8, 9. However, these are probably unimportant quantitatively.

**Miss Beatrice Rubin, head of the OPD food clinic offered invaluable help in the clinical development of this method.

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Submitted June 29, 1951.

CLASS II. Each serving is ¾ cup unless specified.

Beets, ½ cup	Parsnip, ½ large
Carrots	Pumpkin
Peas, any, ½ cup	Squash, winter

CLASS III. Rich in starch—to be used only as bread substitute. See under carbohydrate exchanges.

Using the above as a basis for prescribing or recording intakes, the physician calculates the total grams of carbohydrate, protein, and fat by the following revised calculation list:

DOCTOR'S DIET CALCULATION LIST

Units C	P	F	(Categories &) Food	Amt.	Grams C	P	F
			(Carbohydrate)				
1	—	—	Sugar, jelly	1 tsp.	5	—	—
2	½	—	10% Veg.	1 serv.*	10	3	—
			(COH—Prot)				
3	½	—	Bread, cereals, 15% Veg.	1 serv.	15	3	—
			(Protein)				
—	1	1	Meat, fish, fowl, 1 egg	1 oz.	—	6	5
—	1	2	Cheese, misc. types	1 oz.	—	6	10
			(Fat)				
—	—	½	Peanut butter	1 tsp.	—	—	2½
—	—	1	Butter, oils, (nuts),** etc.	1 tsp.	—	—	5
—	—	1	Cream, Med., sour (20%)	2 tbsp.	—	—	5
—	—	2	Cream, Heavy (40%) Swt.	2 tbsp.	—	—	10
			(COH, Prot., Fat)				
2	1	2	Milk, 1 glass	240 cc.	10	6	10

Calcium: 1 day's requirement = 1 gram; 1 oz. Cottage cheese = .025 gm.
Calcium equivalents: ¼ gram = 240 cc. milk, 1 oz. misc. cheese or ¾ oz. cream cheese.

COMMENTS

*1. 1 serving = ½ cup, 1 saucedish or 100 gm.

**2. Nuts, by specified number.

3. Cider, beer, carbonated drinks = 10% sugar.

4. Meat should be lean. For pork, add 1 tsp. fat per ounce.

5. Cheese: Cottage has no fat; cream cheese has only 3 gm. protein/oz.

6. Milk: Evaporated is twice concentrated: 20-12-20 per 240 cc. Ice cream: ½ cup or a scoop is approx. a glass of milk plus 10 gm. sugar.

It can be seen that this diet has been simplified to conform to a unit system such that 1 unit of carbohydrate is 5 grams (or 1 teaspoon) of sugar, 1 unit of protein is 6 grams (or that contained in one ounce of the predominantly protein containing foods) and 1 unit of fat is 5 grams of butter. The unit values are recorded only in order to provide the key to the method of construction of the C, P, F figures and to help form a schema for memorizing the latter. The comments help amplify and increase the accuracy of the list.

To test this method, dietitians in our clinic recorded the routine food intake of 10 consecutive diabetic patients in servings. Then, separate dietitians* calculated the total C, P, F content in grams using the following references for calculation: Stern (2), Duncan (11), a simplified method based on Stern's figures and the unit system just described. The actual average times consumed were 8, 5, 2, and ½ minutes respectively. The advantage of this unit system was even greater than could be expressed in figures, since it could easily be committed to memory.

The accuracy of the unit system was tested by using Stern's figures as an index (2). The accuracy was within the limits of 5% for practically all the totals and never outside of 10%. This is well within the accuracy of the variations of the actual content of the foods and the errors of measuring them by the serving technique (12).

The actual formulation of the patient's diet may be by the use of basic diets as illustrated by recent publications of the American Diabetes Association (13a, b). But, the calculations of these initial diets or of subsequent changes in following up the patients is rendered relatively simple by this unit calculation method. Clinical experience in the use of this method since 1949 has amply confirmed the original impressions concerning its simplicity and convenience.

*Misses Beatrice Rubin and Geanne Spelman.

DISCUSSION

Diet therapy in diabetes mellitus has evolved slowly through many decades of changing concepts. The reason for our success in treating this disease resides in the fact that the carbohydrate tolerance remains reasonably constant* from day to day in most diabetics as in normals. This tolerance is a result of the activity of a myriad of enzymes and hormones. Let us express the diabetic therapeutic problem as a rough formula valid only for a given individual and in which "k" represents the carbohydrate tolerance:

Fixed endogenous insulin x Diet (C, P, F) = k x blood sugar level. In the normal, the pancreatic insulin content is large enough to support overnutrition and with its responsiveness can accommodate wide variations in both diet and "k". In the diabetic it is fixed and unresponsive, so that there is a close relationship between the dietary carbohydrate and the resultant blood sugar levels.

With the advent of manufactured insulin, the formula could be rewritten as follows:

Variable Exogenous Insulin x Diet (C, P, F) = k x blood sugar level. By this exogenous insulin supplement, the patient was forthwith removed fom the danger area of inadequate carbohydrate utilization and acidosis. In addition, it enabled us to prescribe a diet adequate to attain a normal weight level. However, when that level was reached by means of a determined daily insulin dose, the necessity still remained for keeping the diet reasonably constant in order to maintain a corresponding constancy of blood sugar level. How constant is the latter? This may be expressed in terms of the observed rise in blood sugar value from the maximum fasting to the maximal postprandial levels in normals: 120 mgm. to 150 mgm. respectively, a difference of 30 mgm. per cent. Postprandial blood sugar values up to 180 mgm. percent, an increase of 30 mgm., in the treated diabetic is commonly regarded as eminently satisfactory. This represents a leeway of 100% in the fasting-postprandial blood sugar difference. The constancy of the diet required to achieve an aim of normoglycemia can be estimated in another way. About 86% of physicians who have this aim of therapy are satisfied from clinical experience that their patients can achieve this goal with the household serving-ex-

*Constancy of diabetic tolerance may be disturbed by complications or by weight change, increasing with undernutrition and decreasing with obesity.

change list technique. And this method is accurate only to 10%. Both the methods and the aims outlined above fall well within the unavoidable natural variations of the carbohydrate content of the food in the diet as previously mentioned.

The effect of food upon the blood sugar of the diabetic involves two quantitative factors: the total glucose equivalent of the food and the velocity of its assimilation (14). The sources of *slowly* available carbohydrate are the ingested non-carbohydrate (protein, fat) foods and the nocturnal gluconeogenesis present in all diabetics as part of a diurnal carbohydrate metabolic rhythm (15, 16). Since the introduction of protamine zinc insulin, the hyperglycemic effect from the latter sources has been minimized in significance. Accordingly, protein and fat have become important largely from the viewpoint of normal nutritional requirements and of weight control.

There remains then the predominantly carbohydrate containing foods which are rapidly assimilated and act as the key factors in the present day control of hyperglycemia. Attempts to simplify dietary measurements and calculations then center on these. Of this group, the vegetables and fruits are particularly variable in carbohydrate content and have presented a barrier to simplification of diet calculations for many decades. The first step in this direction was the introduction of the serving method as a substitute for weighing. This change was a recognition of the fact that slight errors of the household serving technique (as contrasted with weighing) did not exceed the natural variations of the carbohydrate content of the food itself (12).

The next step was the introduction of substitution lists. This gives the patient a convincing illusion of variety at the price simply of taking his food in arbitrarily defined individual portions. Yet, by classifying the vegetables in groups which are uniform in carbohydrate content (i.e. 5, 10, 15%), it simplifies the calculations for the physicians. The same is done for fruits to a more extreme degree, resulting in only one list.

The method introduced here is a step forward in the direction of further simplification of the physician's calculations to conform to that which had already been afforded the patients. It removes the scientific paradox of the use of two orders of accuracy in the same procedure. Since the present method was devised, the American Diabetes Association has likewise introduced a simpler technique of diet calculation. However, that method is not in the form of a unit system, it is not as all inclusive and it introduces a slight loss of accuracy due to the omission of the 3 per cent vegetables from the calculations entirely (13a, b).

Whichever diet calculation system is used, there has occurred an important change in emphasis from a policy of the maximum possible accuracy to one of the minimum constancy required. This standard of reasonable constancy not only is justified scientifically but by clinical trial it works as well as the old. More important it may help remove important psychological barriers to better diabetic control on the part of the family physician who sees most of this country's diabetics. The new simplicity will encourage him to treat such patients in a more satisfactory manner, for the patient's desire to maintain his diet can only be a projection of the doctor's enthusiasm in the same direction.

SUMMARY

1. A simplified method for the calculation of diabetic diets has been devised, utilizing a unit system of construction for the purpose of easy memorizing.

2. Clinical application of this method has confirmed its convenience and accuracy.

3. The historical and experimental background of the evolution of this modern simplified diabetic diet is discussed.

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CLINICAL STUDIES OF BLOOD LIPID METABOLISM
I. NORMAL BLOOD LIPID VARIATIONS OF PHOSPHOLIPIDS, NEUTRAL FATS, TOTAL LIPIDS, AND LIPID FRACTION PERCENTAGES

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MUCH HAS BEEN expressed of the effect of lipids upon conditions such as atherosclerosis, arteriosclerosis, coronary disease, and liver pathology. Experimental and clinical studies have been published with no final and with varied conclusions. The lay press has stressed these indefinite results to such an extent that patients request and demand to know "The values of their fats in the blood."

Without a doubt, changes in the arteries of animals have been produced experimentally simulating atherosclerotic processes in humans.

Blood studies, especially of cholesterol, are numerous. Other lipid substances such as phospholipids (phosphatides) and fatty acids are less frequent. Some are so persistent as to state, with a note of finality, that a ratio of these substances, for instance, phospholipids to cholesterol or vice versa, in one way or another speak for or against atherosclerosis or overt coronary disease. The more exact and most recent work is that of Gofman and his associates with their qualitative study of lipomicrons (any fat particle) and chylomicrons (large fat particles) by ultra centrifugation. This awaits further confirmation for practical clinic usage.

Before any discussion of the clinical value of lipids is mentioned, it seems in order to define lipids; the various types commonly encountered clinically; their function; and normal variations, at this stage of our knowledge. In subsequent publications, the author will attempt to evaluate findings in certain clinical conditions.

CLASSIFICATION OF LIPIDS (1)

The term "lipid" (2) is used to designate those substances which, in their general properties and particularly in their solubilities resemble fats.

1. *True fats and oils*, triglycerides of fatty acids.
2. *Nitrogen-containing lipids*, substances of a fat-like nature, yielding on hydrolysis fatty acids or derivatives of fatty acids and containing nitrogen.
   - A. *Phospholipids*, nitrogenous lipids containing phosphorus.
     - a. *Phosphatides*, triglycerides in which one fatty acid is replaced by a phosphoric acid tester. Each molecule contains two molecules of fatty acid to one of phosphoric acid. To this group belong lecithin and the cephalins.
     - b. *Sphingomyelins*, like the phosphatides contain both nitrogen and phosphorus, but only a single molecule of fatty acid to each molecule of phosphoric acid.
   - B. *Cerebrosides*, substances containing fatty acids, nitrogen, and a carbohydrate group, but no phosphorus. Of these, at least two members have been identified, phrenosin and kerasin.
3. *Unsaponifiable materials*, having no close chemical relation to fat except similar solubilities, and no functional relationship except that some members form esters with fatty acids.
   - A. *Sterols and Steroids*. Compounds having a perhydrocyclopentophenanthrene nucleus.
     - a. cholesterol and its immediate derivatives.
     - b. steroid vitamins and provitamins.
     - c. steroid hormones.
     - d. bile acids.

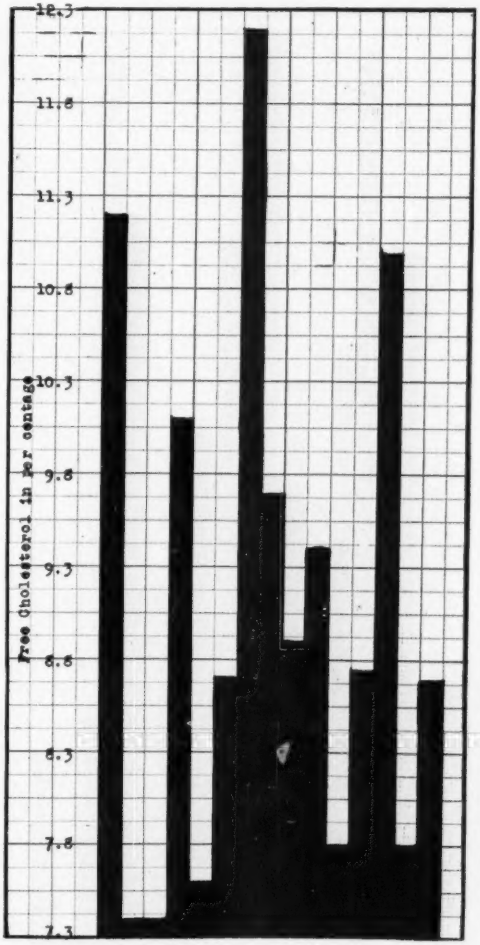

Fig. 1: Histogram showing the percentage of serum free cholesterol in terms of total lipid concentration in normal male and female patients.

From the Medical Services of the Beth Israel Hospital and the New York Medical College, Flower and Fifth Avenue Hospital (Metropolitan Hospital Division).

Submitted July 7, 1951.

B. *Other fat soluble vitamins and provitamins.*
   a. carotenes and A vitamins.
   b. tocopherols and E vitamins.
   c. naphthaquinones and K vitamins.

C. *Unidentified nonsaponifiable materials.*

GENERAL TERMINOLOGY

Ester—is any compound formed from an alcohol and an acid by the removal of water.

$CH_3COOH + C_2H_5OH = CH_3COOC_2H_5 + H_2O$

Acetic acid + alcohol = ethyl acetate (ester)

Glyceride—is an organic acid ester of glycerol (glycerin). The natural fats are glycerides of the higher fatty acids and usually are mixed glycerides.

$H_2C - O - CO - C_{17}H_{35}$
$H\ C - O - CO - C_{17}H_{35}$
$H_2C - O - CO - C_{17}H_{35}$

(Tristearin)

A Simple Glyceride

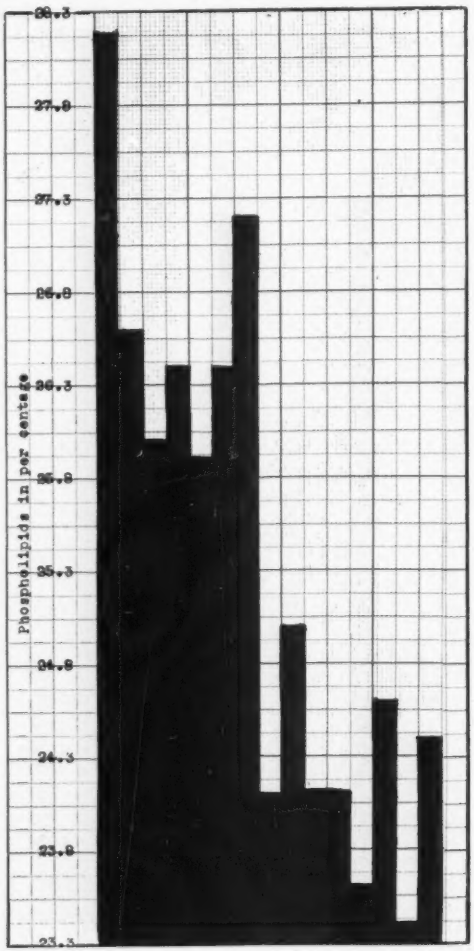

Fig. 2. Histogram showing percentage of phospholipids, as part of total lipid concentration, in normal patients.

Fats (3)—are esters of fatty acids and glycerols (glycerin) that contain mixtures of glycerides which are esters of glycerol and one or more fatty acids.

$H_2C - O - CO - R_1$
$H\ C - O - CO - R_2$
$H_2C - O - CO - R_3$

General formula for fat. R_1 etc. nomenclature for fatty acid radical.

Fatty Acids (3)—are monobasic aliphatic (pertaining to an oil) acid formed by the oxidation of a primary alcohol and having the formula $CnH_{2n}O_2$. Example: $C_{15}H_{31}COOH$ (palmitic acid) or $(C_{16}H_{32}O_2)$.

Some of the fatty acids found in fats which occur more or less commonly are acetic (vinegar), butyric (butter), arachidic (peanut oil), etc. The most important and most widely distributed fatty acids are stearic, palmitic, and oleic. The fatty acids form soaps with metals or alkalies, as:

$C_3H_5(O\text{-}CO\text{-}C_{17}H_{35})_3 + 3NaOH = 3C_{17}H_{35}COONa + C_3H_5(OH)_3$

stearin + sodium hydroxide = sodium stearate (soap) + glycerol (glycerin) and esters with alcohol

$CH_3COOH + C_2H_5OH = CH_3COOC_2H_5 + H_2O$

acetic acid + alcohol = ethyl acetate (an ester).

Neutral fats (4)—are defined when all three alcoholic groups of glycerol are esterified with fatty acids (R_1, R_2 or R_3) which may be either saturated or unsaturated.

$H_2C - O - CO - C_{15}H_{31}$
$H\ C - O - CO - C_{15}H_{31}$
$H_2C - O - CO - C_{15}H_{31}$

Palmitin (neutral fat)

The general structure of fats is that of glycerol esters. They may be split in the bile into glycerin (glycerol) and fatty acids which may combine with choline and phosphoric acid to form the phospholipid lecithin.

Lipid Phosphorus (5)— is one of the phosphorus fractions existing in blood in organic combination. Upon extraction of blood with alcohol-ether lipid phosphorus is obtained and is considered in the alcohol-ether organic, soluble class.

Phospholipids (Phosphatides)—is a nitrogenous lipid containing phosphorus which on hydrolysis yields fatty acids, glycerin, and a nitrogenous compound. They are esters of orthophosphoric acid. Lecithin is the best known example.

$H_2C - O - CO - R_1$
$H\ C - O - CO - R_2$
$H_2C - O - P(=O) - O - C_2H_4 - N^{+}(CH_3)_3$ (OH)

Alph-lecithin

Lecithin (6)—is a common cell constituent and is considered to play a part in metabolism of fat. Unlike true fats, it contains nitrogen and phosphorus. In the industries, many thousands of pounds of lecithin, obtained from soy-beans are used as an emulsifier and in the manufacture of candies, chocolate, cocoa, margarine, medicines, and even in the dyeing of textiles.

Sterols—are complexed monohydroxy alcohols which are unsaponifiable substances having no close relation to fats. The most important one concerned is *cholesterol*, which exists in the body in two states, free and esterified (combined with fatty acids).

$C_{27}H_{45}O$—cholesterol

Lipotropic agents—are substances having an affinity for fats or oils and thus acting on fat metabolism. Example:

$HO - CH_2 - CH_2 - N(OH)(CH_3)_3$

Choline (ethanol trimethyl ammonium hydroxide).

Choline—is a base comparable to sodium hydroxide. It is important in preventing the accumulation of fat in the liver and is generally regarded as a constituent of the vitamin B complex.

OCCURRENCE OF LIPIDS

Individual members of lipids show large individual variations in solubility, but as a class the lipids are readily distinguishable from the carbohydrates and the proteins, the other two great groups of naturally occurring compounds. They are very wide-spread in nature, being found in all vegetable and animal matter. Some members of this group such as the phosphatides and sterols, are found in all living cells where, with the proteins and carbohydrates, they form an essential part of the colloidal complex of protoplasm. Complex lipids are also found in large quantities in brain and nervous tissues, thus indicating the important role these substances must play in the living organism. Other lipids, such as the fats, and oils, represent the chief form in which excess foodstuffs are stored in the animal body. They arise from ingested lipids and from the metabolism of carbohydrates and proteins, and are stored in fat deposits, such as the subcutaneous connective tissue, the intermuscular connective tissue, the omentum, etc., where they act as heat insulators and as reserve supplies of energy (7).

FUNCTION OF LIPIDS IN GENERAL

Dietary lipids which are ultimately to be metabolized in the body consist for the most part of glycerides of fatty acids. One of the chief functions of dietary fat is to provide a large available reserve of food and essential fatty acids to the organism. Digestion of fats is determined by 1) the normal presence of the digestive fluids in the intestine and 2) an adequate period of time for this digestive process to proceed. Sinclair (8) postulated the following equilibrium as existing in the intestinal wall: fatty acids ⟶ phospholipids ⟶ fat.

There is a specific phospholipid in the intestinal mucosa which occupies an intermediary position between fatty acids and neutral fats. All of plasma phospholipids are the choline type. Therefore, transport of fatty acids by way of phospholipids involve only those phospholipids that contain choline, which is the nitrogenous basic constituent of lecithin. Lecithin is the form in which fat is transported from blood to tissues and in the opposite direction.

While fatty acid in the blood may in part be transported as phospholipids, an important role in this process is also played by the esters of cholesterol and of glycerol (neutral fat) (9).

Protein may play a role in aiding lipid transport in the blood as may be shown that blood lipids are found concentrated in the beta globulin fraction when plasma is fractionated by physico chemical methods (10, 10a). Alteration in total blood lipids are a reflection of changes in the concentration of the individual constituents which comprise the total lipid fraction of the blood.

FUNCTION OF INDIVIDUAL LIPIDS

Cholesterol (11, 12) is an essential constituent of all cells and fluids of the body. It is a precursor of cholic acid and cholestenone and also functions with the bile acids and salts in facilitating the absorption of fatty acids. It is an important means of transportation of fatty acids in the blood, through the formation of cholesterol esters. It is present in highest concentration in the adrenal cortex and is biological precusor of steroid hormones. It is an important source of vitamin D by irriadiation of the skin, with the formation of activated 7-dehydrocholesterol. It may be involved in cell permeability and possibly in immunologic reactions.

SOURCES FOR SERUM CHOLESTEROL

The cholesterol in the body is derived from two sources, that ingested in the diet and that obtained by endogenous synthesis. The only important exogenous dietary sources are certain animal fats and products, including milk, butter, cheese, and egg yolk, and animal organs such as brain and liver; certain sea foods such as oysters are also fairly good sources (13). Endogenous cholesterol has been known to be synthesized in the liver. Gould (14) by studying tissues after administration of radio active carbon compounds has concluded that synthesis of cholesterol takes place also in the intestinal mucosa and skin but not in the aorta.

The liver synthesizes cholesterol at the approximate rate of 0.3 grams per day which is believed to balance the rate at which cholesterol is normally excreted. Cholesterol, whether contained in the diet or produced by the liver, passes through the small intestine. Here, one of two things happens: It is absorbed, or is passed on to the colon and excreted. By reducing absorption, excretion will be increased. Since the fatty acids of dietary fats greatly promote the absorption of cholesterol by converting it to cholesterol esters, a low fat diet would greatly reduce cholesterol absorption and thus greatly aid in its elimination. In addition, a low fat diet also has been reported to increase the excretion of bile acids and since these bile acids are made by the liver from cholesterol, the indirect effect might be to reduce cholesterol.

Exogenous and endogenous cholesterol are present in the intestine and react with the fatty acids. Some free cholesterol is transformed into coprosterol and excreted through the feces. The esterified form is absorbed and is carried to the liver where the cholesterol in part is "liberated," the fatty

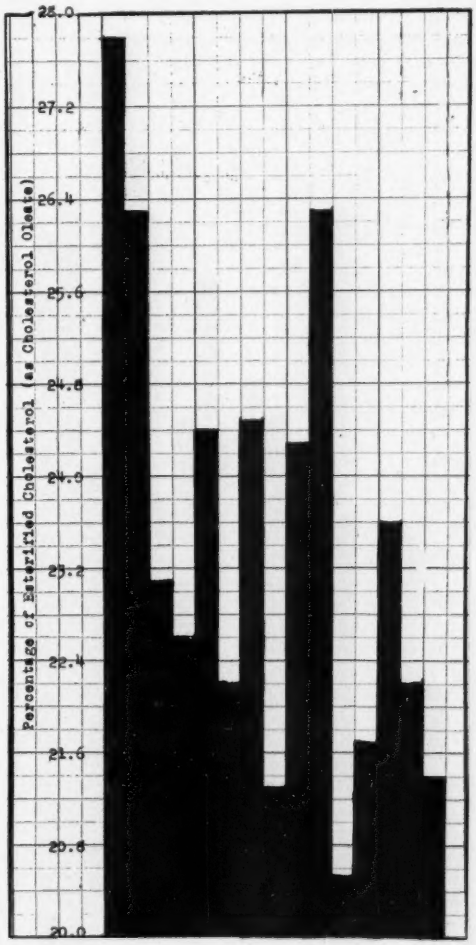

Fig. 3: Percentage of serum esterified cholesterol (as cholesterol oleate) of total lipid concentration in normal individuals.

acids entering into combinations with phosphoric acid and choline, which may be present within the lumen of the intestine to form lecithin. Some fatty acids give rise to acetates, considered to be the building blocks for cholesterol synthesis.

STEROL=CHOLESTEROL ESTER AND ESTERIFIED CHOLESTEROL

By means of hydroxyl group on carbon (3) cholesterol combines with fatty acids to form esters (15). The alcoholic hydroxyl, which can be esterified with different fatty acids by means of an esterase, may be split by reverse action. The esterification of cholesterol changes its physical properties, which not only have an influence on the absorption and transportation of this substance in the tissue fluids but are also important for the composition of the cell lipids. A cholesterol esterase also seems to be present throughout the body. The liver plays an important role in regulating the ratio of free cholesterol to cholesterol esters as it manifests itself in the serum of men and animals; 60-70% of the total cholesterol is normally present as cholesterol esters in the serum.

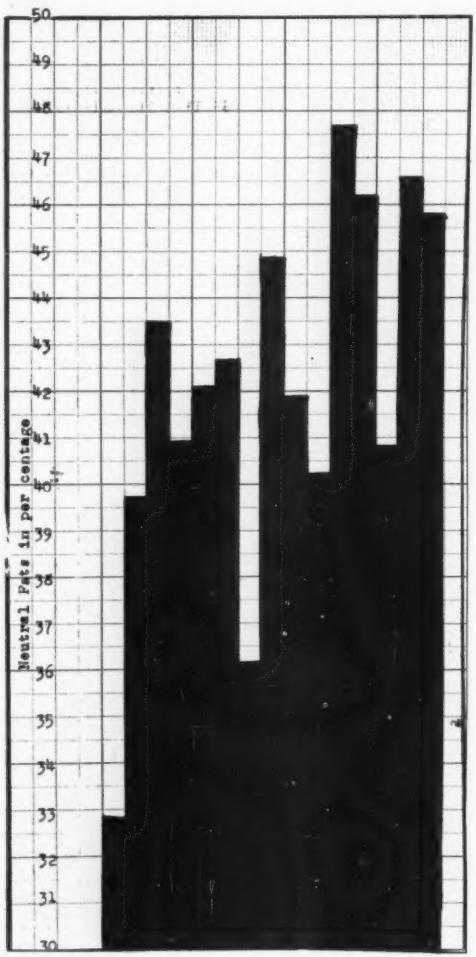

Fig. 4: Percentage of serum neutral fats, in terms of total lipid concentration in normal male and female patients.

Sperry (16) showed that incubation of normal serum increases the ester fraction of cholesterol. He, therefore, assumed that normal blood contains a cholesterol esterase, which may be responsible for maintaining the normal ratio of free cholesterol to cholesterol ester. It is more probable that the cholesterol esterase, which is found in organs, especially the liver, may be responsible for the ratio in the blood. Willibald Klein found that cholesterol esterase in the duodenum originates from pancreatic secretion. He stated also that this esterase is not identical with other esterases (17).

Cholesterol probably enters into complex molecular combination with protein in the parenchyma of the liver. Thus, there are released into the blood stream four varieties of cholesterol, derived fundamentally from either exogenous or endogenous cholesterol.

1. Synthesized (endogenous).
2. Originally ingested (exogenous) now nonesterified.
3. Giant molecular cholesterol-protein complex.
4. Esterified cholesterol (hepatic and intestinal).

Some of this cholesterol is returned to the liver to be secreted in the bile along with cholesterol which enters the bile directly from the liver.

Thus the circuit intestine-liver-blood stream-bile-intestine—the so-called entero-hepatic circulations—is complete.

PHOSPHOLIPIDS AND CHOLINE

Phospholipids are a vital means for transporting fat around the body and for preventing it from infiltrating the arteries, the liver, or other organs. The principal type is lecithin, a substance closely resembling fat in chemical structure, except for this vital difference; it contains choline, linked by phosphoric acid. This choline is a vital substance, a member of the vitamin B complex and specifically recognized as a lipotropic agent, that is, it is essential to keep fat on the move. From choline, supplied by the diet or medicinally, the body can make lecithin and other phospholipids. Liver is the main source of the plasma phospholipids. By radio phosphorus as a tracer, the level of the plasma phospholipids is a measure of the amount of new phospholipid being formed. If the level is high, there is an overproduction of the phospholipid by the liver rather than a piling up due to biliary obstruction or decreased breakdown of the phospholipid molecules by the tissue. This has been found to be true no matter what the cause of the hyperlipemia in all the pathological states studied (18).

The phospholipids are the major form in which fatty acids are transported about the body. There are several kinds of phospholipids: lecithins represent about 50 percent, cephalins about 40 percent, and sphingomyelins about 10 percent of the phospholipids in the blood; the red cells contain even more phospholipids than the plasma, but it is the latter which is believed to be mainly involved in the transportation of fat to the adipose tissues.

In lecithin, the distinguishing chemical entity is choline, while in cephalin it is ethanolamine. The latter is closely akin to choline. Choline is also a component of sphingomyelin.

Animals on a diet free from phospholipids can produce their own from choline. Therefore, choline is looked upon as the lipotropic agent par excellence. From 1 Gm. of choline the body can make 6 Gm. of lecithin, and probably an equal amount of cephalin.

In the ordinary diet choline is present chiefly in the form of phospholipids; since these are fat-soluble substances, they are most plentiful in fats rich in cholesterol, such as eggs, brain, kidney and liver. Consequently, the patient who tries to keep away from cholesterol finds himself automatically cut off from the main sources of choline.

A low fat diet, while it may be poor in choline, need not cause any deficiency of lipotropic factors, provided it be rich in animal proteins, since the latter supply an abundance of methionine, which the body can convert into choline.

Dietary deficiency of choline and other lipotropic factors is known to result in increased production of fat by the liver from carbohydrates. This not only causes fatty infiltration of the liver but also causes the accumulation of cholesterol.

Dietary deficiency of such "lipotropic" substances as lipocaic, methionine, choline, inositol and animal protein causes fatty liver and cirrhosis in animals under certain conditions. The evidence relates these events to a defect in phospholipid synthesis by the liver that accumulates fat in large amounts. Phospholipid synthesis is stimulated by administration of

Case Number	Age	Sex	Height	Weight	Status	Blood Serum Lipids ---- mgm. per 100 ml.										Ratio of phospho-lipids to Cholesterol	Ratio of total cholesterol to phospholipids	Lipid Fraction %				Liver Function Tests							Diagnosis
						Lipid Phosphorus	Phospholipid as lecithin	Cholesterol						Neutral Fats	Total Lipids			Cholesterol				Thymol Turbidity (units)	Ceph. Floc.		Total proteins	Albumin	Globulin	A/G Ratio (-11)	
								total	ester as part of cholesterol	% of total	free	% of total	esterified(as cholesterol oleate)					free	esterified (as cholesterol oleate)	phospholipids as lecithin	Neutral Fats		24 hr.	48 hr.					
2	42	M	60	116	asthenic short	9.2	230	226	136	60.1	90	39.9	227	268	815	1.01	0.98	11.2	27.8	28.2	32.8	2	0	0	6.94	4.42	2.52	1.7	Psychoneurosis
6	69	M	63	147	sthenic short	8.8	220	190	130	68.4	60	31.6	217	328	825	1.15	0.86	7.4	26.3	26.6	39.7	0	0	0	6.84	4.62	2.22	2.08	Gastritis
8	51	M	65	161	sthenic	9.4	242	196	129	65.8	67	34.2	215	404	928	1.23	0.80	7.4	23.1	26.0	43.5	3	0	0	6.94	4.42	2.52	1.71	Functional dyspepsia
17	51	F	64	120	sthenic	8.4	210	186	108	58.0	78	42.0	180	325	793	1.12	0.87	10.1	22.6	26.4	40.9	2	0	0	7.10	4.74	2.36	2.0	Arthritis
19	41	F	62	181	hyper-sthenic	9.2	230	196	130	66.3	66	33.7	217	374	887	1.17	0.85	7.6	24.4	25.9	42.1	2	0	0	6.84	3.96	2.88	1.30	Psychoneurosis
28	27	F	60	111	asthenic	8.9	222	184	112	60.9	72	39.1	187	359	840	1.20	0.82	8.7	22.2	26.4	42.7	2	0	0	6.48	4.22	2.26	1.86	Psychoneurosis
30	40	M	62	150	sthenic short	7.9	197	193	106	54.9	87	45.1	177	261	722	1.02	0.97	12.2	24.5	27.2	36.1	2	0	0	6.82	4.38	2.44	1.80	Psychoneurosis
31	72	F	58	77	asthenic	8.8	220	200	123	61.5	77	38.5	205	410	912	1.10	0.90	9.7	21.3	24.1	44.9	0	0	0	7.39	4.89	2.50	1.80	Functional dyspepsia
43	44	M	68	163	sthenic	8.4	230	214	134	62.6	80	37.4	223	384	917	1.07	0.93	8.9	24.3	25.0	41.9	3	0	1	7.18	4.13	3.05	1.35	Normal
45	22	F	60	108	sthenic	7.8	195	203	128	63.0	75	37.0	213	325	806	0.96	1.04	9.4	26.3	24.1	40.2	2	0	1	6.84	3.96	2.88	1.30	Psychoneurosis
51	50	F	64	172	hyper-sthenic	9.4	235	200	120	60.0	80	40.0	200	465	974	1.17	0.85	7.8	20.5	24.1	47.7	0	0	0	7.36	4.18	3.18	1.31	Menopause
53	34	F	61	110	sthenic	8.8	220	200	122	61.0	78	39.0	203	431	932	1.10	0.90	8.5	21.7	23.6	46.2	2	0	0	6.68	3.78	2.90	1.30	Normal
56	47	F	64	116	asthenic	7.9	198	202	114	56.4	88	43.6	190	328	804	0.98	1.02	11.0	23.6	24.6	40.8	2	0	0	6.86	4.16	2.70	1.50	Asthenia; hemorrhoids
57	50	M	67	157	sthenic	8.2	205	184	116	60.1	68	39.9	193	407	873	1.11	0.89	7.8	21.8	23.4	46.6	3	0	1	6.99	3.74	2.75	1.36	Normal
62	54	F	67	148	sthenic	8.7	217	192	115	59.8	77	40.1	192	411	897	1.13	0.88	8.7	21.4	24.1	45.8	4	0	1	6.03	3.85	2.18	1.76	Psychoneurosis
arithmetic mean			63	136		8.65	218	197	121	61.2	76.2	38.8	202	365	861	1.10	0.90	9.1	23.5	25.3	42.1	2.2	0	.26	6.85	4.23	2.62	1.61	

Table I. Lipid variations of phospholipids, neutral fats, total lipids, lipid fraction percentages and liver function tests in fifteen normal patients, male and female.

choline or of methionine, the latter providing methyl groups for the synthesis of choline. This fundamental work does not specifically indict deficiency of any of these nutrients in the pathogenesis of liver disease in man although, as pointed out above, improper food consumption unquestionably plays an important role. Generally, diets of persons in whom fatty liver and cirrhosis develop, whether associated with alcoholism or not, are, as noted above, deficient in protein, especially that of animal origin. This deficiency includes methionine, choline, and the other nutrients usually classed in the vitamin B complex. The evidence incriminating dietary factors in the pathogenesis of liver disease in animal experiments is necessarily more specific than that in man, but the two bodies of evidence are compatible.

SIGNIFICANCE OF LIPOPROTEIN COMPLEX

Chylomicrons are minute fat globules in which form fat is absorbed from the alimentary tract. The fat contained in the diet enters the blood stream by gateways provided in the small intestines. Some of it escapes the splitting action of the bile and may penetrate directly into the lymphatic outposts, called the lacteals, situated in the intestinal projections known as villi. The rest is principally split into fatty acids and glycerine. Then fatty acids enter into the composition of lecithin and other "phospholipids" and combine with relatively insoluble cholesterol in the bile and in the digestive food itself to form cholesteryl esters which are readily absorbed into the lymph channels. These take the fats and other lipids to the blood stream, where they are suspended in particles about one micron in diameter known as the chylomicrons.

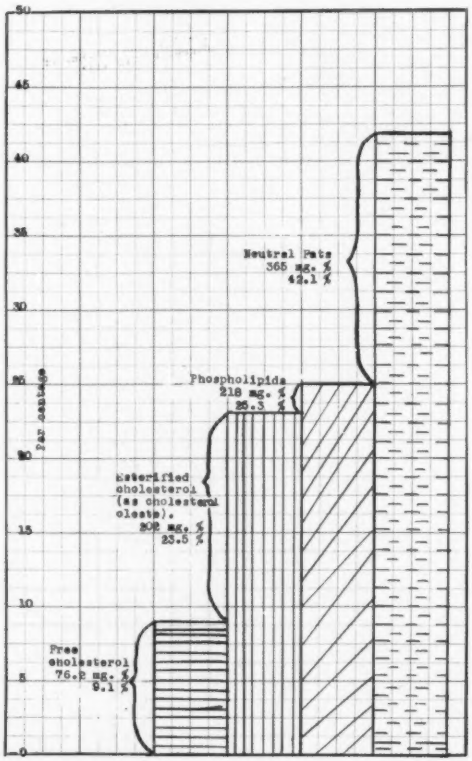

Fig. 5: Graphic representation of arithmetic mean of serum lipid pattern of normal male and female patients. Percentages are in terms of total lipid values. Milligram percent per 100 ml. serum, as determined.

Gofman and his associates (19, 20), by analytical ultracentrifugation, had been able to study quantitatively the entire spectrum of lipid and lipoprotein components of sera. Four classes of chylomicrons have been described on the basis of the Svedberg flotation rates:

Sf 3-8 Normal components of all sera.
Chiefly phospholipids, lipoprotein and cholesterol.
Relatively constant for each individual, vary between individuals. Do not fluctuate with meals or disease.

Sf 10-20 Stable on given diet, not affected by individual meals.
Contain 30 per cent cholesterol.
Possibly related to the occurrence of atherosclerosis.
Sometimes Sf 20-30 are found with the Sf 10-20 group.

Sf 30-70 Major fraction during alimentary lipemia.
Greatly modified by meals.

Sf over 75 Represent the chylomicrons and other large aggregates.
Increased after fat meals and are part of alimentary lipemia.

FUNCTION OF THE LIVER IN FAT METABOLISM

Liver plays an important part in the metabolism of fat as evident by the following facts: (1) The liver extensively desaturates fatty acids (21). The fatty acids in the liver are more unsaturated than the fatty acids found in other tissues (22, 23). Saturation of unsaturated fatty acids has also been shown to occur, producing evidence that saturation and desaturation of fatty acids in the mammalian organism is a physiological reversible process (24). (2) Neutral fat or cholesterol esters may accumulate more in the liver than in

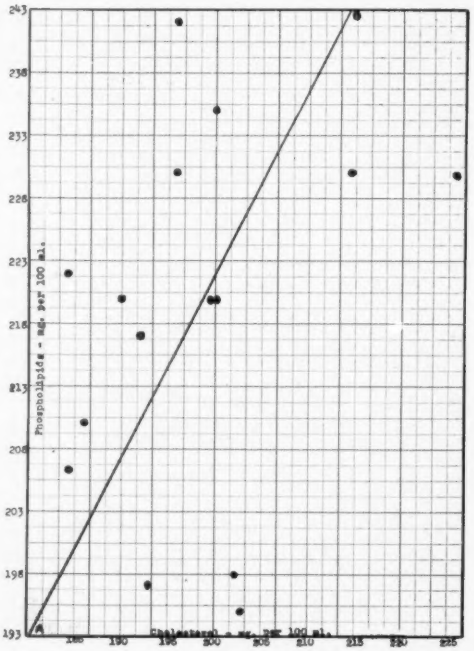

Fig. 6: Scatter graph of relationship between phospholipids and cholesterol in fifteen normal individuals. A-B represents range arithmetic mean.

any other tissue. (3) Ketogenesis occurs chiefly in the liver as a result of the oxidation of fatty acids and is the chief site of formation of ketone bodies (25). (4) The rate of phospholipid turnover in the liver is more rapid than in any other tissue, with the possible exception of the intestinal mucosa during fat absorption. The liver appears to act as a sorting point for fatty acids and a great central laboratory in which phospholipids for the tissues are assembled (26). (5) With respect to steroids, the liver exercises three functions: a) The excretion of cholesterol in the bile; b) The formation and excretion of cholic acid; c) The destruction or inactivation by conjugation of steroid sex hormones. The liver esterifies, synthesizes, stores, and destroys cholesterol (27).

METHOD OF STUDY AND MATERIAL

Patients were chosen who were clinically diagnosed as not suffering from any organic disease especially of the cardio-vascular and coronary systems. The diagnoses were mostly functional dyspepsia and psychoneurosis. No food nor liquids were permitted after the evening meal of the preceding day. Fasting, non-oxalated blood was obtained the following morning, being certain that the patient was at ease, not following any exercise nor effort. Duplicate samples were determined. At least 15 cc. of blood were drawn for lipid fraction and liver studies. The lipid phosphorus (lipid esters of phosphoric acid) was determined by the Youngburg modified digestive method (28). As mentioned above lipid phosphorus was one of the phosphorus fractions existing in the blood in organic combination (5).

It has been shown that the average blood phospholipid contains four percent of phosphorus. Therefore, multiplying by the figure 25 will give the approximation of the weight of the blood phospholipid fraction. Since phospholipids are present in the blood mostly in the form of lecithin, the molecular weight of lecithin is utilized for the determination of phospholipids.

$$\frac{\text{Molecular weight of lecithin (805.7)}}{\text{Atomic wt. of phosphorus (31.2)}} = 25.$$

Total lipids were calculated by the gravimetric modified Bloor method (29).

Total cholesterol and cholesterol esters were determined by the Leiboff method (30). The term cholesterol ester as used clinically is the amount of cholesterol not precipitated by digitoxin and is expressed in terms of cholesterol. In order to express the value of cholesterol ester in terms of actual weight, a factor of 1.67 is utilized. This figure is obtained by dividing the molecular weight of cholesterol oleate by the molecular weight of cholesterol. It is customarily accepted that most of the cholesterol ester of the blood is in the form of cholesterol oleate. This factor of 1.67 is applicable to cholesterol oleate and stearate.

$$\frac{648\ (\text{Wt. of 1 mol. cholesterol} + 1\ \text{mol. oleic acid}\ (-H_2O)}{384\ (\text{Molecular weight of cholesterol})} = 1.67.$$

Cholesterol ester (as cholesterol) $\times$ 1.67 = actual weight of cholesterol ester in mgms. or esterified cholesterol as cholesterol oleate (termed esterified cholesterol by some).

At the present time, there is no practical method to determine neutral fats directly. Neutral fats are ob-

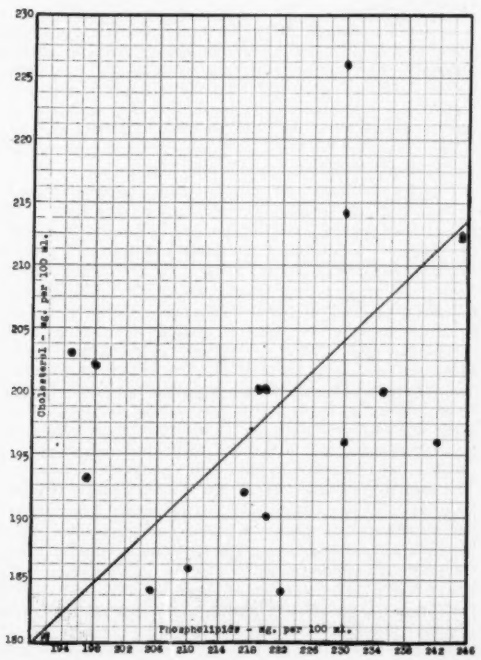

Fig. 7: Scatter diagram of relationship between normal cholesterol and phospholipids. A-B represents range of arithmetic mean.

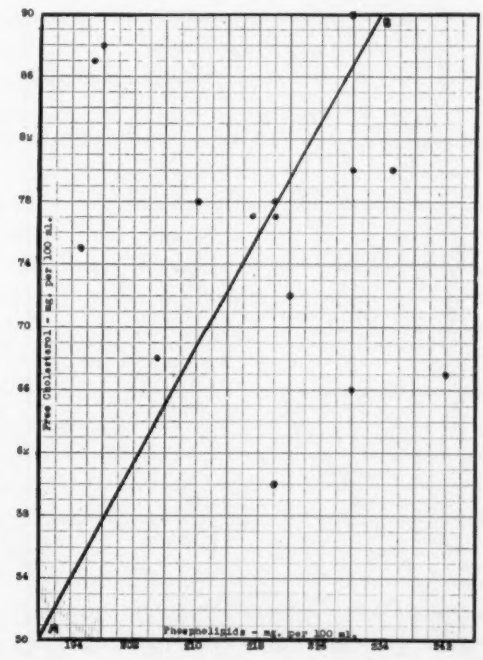

Fig. 8: Scatter graph showing relationship between free cholesterol to phospholipids in normal individuals. A-B represents arithmetic mean.

tained indirectly by subtracting from the total lipid values, the weights of the phospholipid fraction, free cholesterol fraction and the esterified cholesterol as cholesterol oleate fraction.

Lipid fraction percentages were obtained by dividing the weights of the various lipid fractions by the total lipids.

Liver function methods performed were those of the thymol turbidity test of Maclagan (31), cephalin-cholesterol flocculation test of Hanger (32) and the total protein, albumin-globulin values by the Tyrosine method of Greenberg (33). Sedimentation values were performed by the Westergren method (34). Complete blood counts were calculated to exclude any blood disturbance. Height, weight and type of constitution were noted.

RESULTS

Fifteen normal patients were studied as controls, which included nine females and 6 males. The average age was 46 years; height 62.8 inches; and weight 135.8 pounds. Sthenic (normal) type of constitution predominated, as well as the female sex. Table I shows the values of each normal patient, as well as the arithmetic mean for the group. Values varied regardless of the sex, age group, or constitutional status. The highest values for total lipids were found in both the young and the old, male or female and were concomitant with the higher values for lipid phosphorus and phospholipids. The highest total lipid values did not occur concurrently with those of the total cholesterol values and were independent of the high values for neutral fats (Table I). The ratio of the cholesterol esters (as cholesterol) 61.2% and free 38.8% of the total cholesterol values were found to be within normal range.

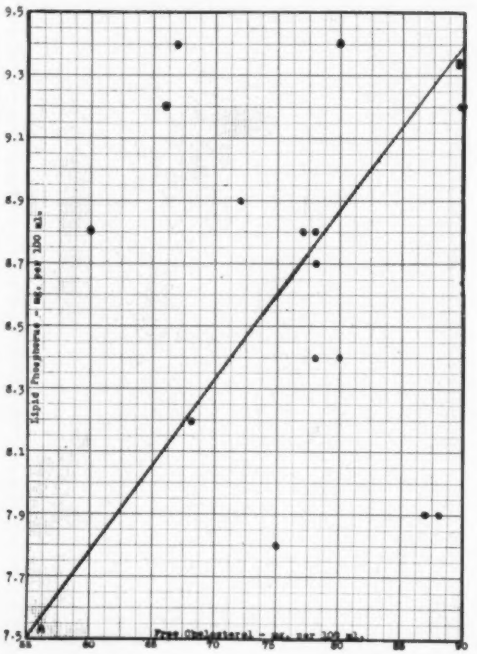

Fig. 9: Scatter graph of lipid phosphorus and free cholesterol in normal male and female patients. A-B represents area of arithmetic mean.

TABLE II

VARIATIONS FROM THE ARITHMETIC MEAN AND RANGE OF THE LIPID FRACTIONS IN MILLIGRAMS PER 100 ML. OF SERUM

Lipid Constituent	Arithmetic Mean	Values Highest	Lowest	Range
Free cholesterol	76	90	60	30
Phospholipids	218	242	195	47
Esterified cholesterol (cholesterol oleate)	202	227	177	50
Neutral Fats	365	465	261	204

Free cholesterol shows the least deviation from the range. Phospholipids and esterified cholesterol reveal practically the same range, while the neutral fats show the highest (see Table II).

TABLE III

VARIATIONS FROM THE ARITHMETIC MEAN AND RANGE OF THE LIPID FRACTIONS IN PERCENTAGES.

Lipid Constituent	Arithmetic Mean	Values Highest	Lowest	Range
Free cholesterol	9.1	12.2	7.4	4.8
Phospholipids	25.3	28.2	23.4	4.8
Esterified cholesterol (cholesterol oleate)	23.5	27.8	20.5	7.3
Neutral Fats	42.1	47.7	36.1	11.6

If the percentage values of the lipid fractions are considered (Table III) the free cholesterol and phospholipids present the same range values (4.8); esterified cholesterol higher (7.3); while the neutral fats are highest (11.6). The variations of the range for neutral fats is much more striking for the molecular weight values, 204 mg. (Table II) than when the percentage values are considered, 11.6 (Table III).

Figures 1, 2, 3 and 4 show the marked normal variations. The graphic representation (figure 1) of free cholesterol appears to vary more than that of neutral fats (figure 4) in spite of the numerical values obtained of the arithmetic mean and range (Tables II and III). Since the graphic representation shows such normal deviation of lipid fractions one must be very cautious to evaluate any therapeutic effects upon abnormal conditions and disease. However, as with any such variation one must compare the "so called" arithmetic mean (average normal) values with those which may be encountered abnormally. The arithmetic mean for lipid fraction percentage is graphically presented in figure 5 showing free cholesterol to be the least (9.1%); esterified cholesterol (23.5%); phospholipids (25.3%). The neutral fats are found to be the highest of the lipid fraction percentage, 42.1% (figure 5). The esterified cholesterol (cholesterol oleate) 23.5% almost approximates the values of phospholipids 25.3%. The free cholesterols were approximately 10% of the total lipid values. The esterified cholesterol (as oleate) and phospholipids constituted about 50% of the lipid values (figure 5). The ratio of the phospholipids to total cholesterol (figure 6) varied more than the ratio of total cholesterol to phospholipids (figure 7). One cannot speak of a constant value for these relationships. It becomes erroneous and dangerous to signal an in-

dividual for atherosclerosis or overt coronary disease because the ratio value of phospholipids to cholesterol or vice versa is above or below 1.00 (35, 36, 37). Even the ratio of free cholesterol to phospholipids (37) (figure 8), or lipid phosphorus to free cholesterol (figure 9), or lipid phosphorus to total cholesterol (figure 10) are not as constant as some report (38).

Thymol turbidity and cephalin-cholesterol flocculation tests showed no abnormal values. The total protein values, with the albumin and globulin partitions as well as the albumin-globulin ratios were within normal range (Table I). The above laboratory data definitely excluded liver pathology and hypoproteinemia.

DISCUSSION

Both the lay and medical publications have been on the increase recently as to atherosclerosis, coronary artery disease, and the values of blood lipid studies. Patients have become so cognizant as to request "blood fat studies." Experimental work has been done producing lesions of atherosclerosis akin to that found in humans by chronic cholesterol feeding.

Numerous publications have mentioned the values of cholesterol and phospholipids, in both normal and abnormal conditions, whether with or without therapy (39, 40, 41, 42, 43). It was felt that normal individuals should first be studied to ascertain the constancy and variations of the blood lipid values. It is important that such determinations be made so as to obtain a base line for comparison.

The results for normals showed the female sex predominated as well as the normal sthenic habitus with no visible influence upon lipid values. One of the highest lipid values (912 mgm. percent) was found in an underweight patient with an asthenic habitus (case No. 31). The average value for total lipid was encountered in a well built individual with a hypersthenic constitution. The ratio of phospholipids to cholesterol was found to be more than 1.00 in a 72 year old female (case No. 31); surely some atherosclerosis must have been present in such an aged individual. If one were to rely on a ratio value of phospholipids to cholesterol of less than 1.00 as being characteristically found in atherosclerosis, one would be misled. The patient (case No. 31) age 72 showed a phospholipid to cholesterol ratio of 1.10, which many observers maintain is found in non-atherosclerotic individuals. If malnutrition were to play a role, a value of less than 1.00 should be obtained in such an underweight person as this 72 year old female (case No. 31).

On the other hand, the lowest ratio of phospholipids to cholesterol (0.96) was found in a young female, age 22 (case No. 45). While it would be exceptional and rare to find overt atherosclerosis in such a young individual, yet such a condition would be considered by some to be present, if the ratio of phospholipids to cholesterol is less than 1.00.

However, one must state that the ratio of phospholipid to cholesterol is 1.00 and above in normals (13 out of 15 patients—86%). But, one cannot deny that some atherosclerosis must be present in some of these normal patients studied as controls, ranging from 50 to 72 years of age. Is it correct to conclude because the phospholipid to cholesterol ratio is 1.00 and above, that no atherosclerotic process is present?

The ratio of cholesterol to phospholipid was found to be less than 1.00 in the same number of instances, 13 out of 15 (86%). The arithmetic mean for the phospholipid to cholesterol ratio was found to be 1.10; while that for cholesterol to phospholipid 0.96. The larger phospholipid to cholesterol ratio occurred where the lipid phosphorus or phospholipid values were comparatively higher than the highest total lipid findings. The higher cholesterol to phospholipid ratio was found where the phospholipid values were lower and independent of the highest total lipid findings.

Complete blood counts excluded any latent or possible haematological disturbances. Liver function tests as mentioned above under methods, excluded any liver pathology, especially protein dysfunction and hypoproteinemia.

Lipid constituents commonly encountered and readily analyzed without any complicated procedures were determined, such as lipid phosphorus, total lipids, total cholesterol and cholesterol esters as cholesterol. The phospholipid values were calculated from the lipid phosphorus values and the neutral fats, as mentioned under methods. It has been shown without any question or any doubt that total cholesterol values do not bespeak for any increased or decreased total blood lipid values. It becomes essential to consider these varied lipid components if we should speak of any such disturbance. Values for phospholipids and cholesterol also are not sufficient to reflect the total fat or lipid constituents of blood. All of these lipid fractions may vary. While it is true that the ratio of the phospholipid to total cholesterol or vice versa are more constant than

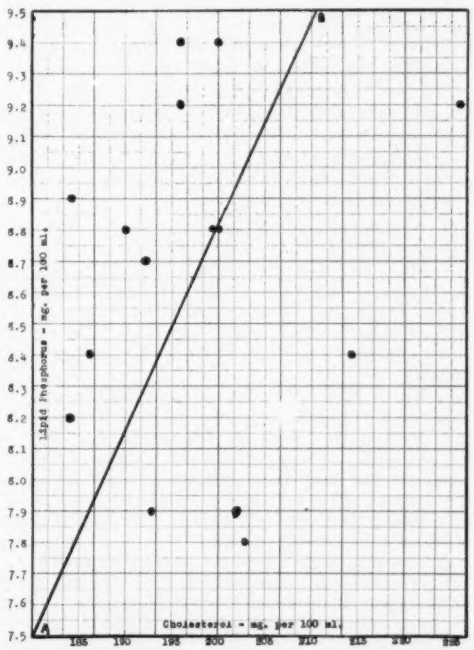

Fig. 10: Scatter diagram of relationship between lipid phosphorus and cholesterol in normals. A-B—region of arithmetic mean.

the individual lipid constituents, yet one may encounter a ratio in normal persons that some may consider characteristic for atherosclerosis or coronary artery disease. One must use caution and discretion as shown above in cases No. 31 and No. 45. Some objections may be raised that the values herein reported are not scientifically accurate since many determinations over a prolonged period may show variant results. While this may be true, yet it is essential as clinicians for us to know the limitations to be employed for clinical practice. Patients will not withstand such extravagance, drawn out laboratory procedures, and time. It is important therefore for practicing physicians to draw the line; utilize his arithmetic mean values, and proceed therefrom.

Animal experimentation and prolonged laboratory work cannot be carried on ad infinitum in clinical practice. Differences in values of the concentrations of lipids in the blood may arise from difference in analytical technique; unreliability of certain methods employed, and the terminology of the constituents such as designating total fatty acids as "fats and neutral fats" or neutral fats as "total fatty acids" (44).

SUMMARY

1. Fifteen normal patients were studied as controls including 9 female and 6 male. The age varied from 22 to 72, with an average of 46 years. Constitutional types were 9 sthenic; 4 asthenic; and 2 hypersthenic.

2. Serum lipid studies included lipid phosphorus, phospholipids (twenty-five times the value of lipid phosphorus), total cholesterol, cholesterol ester, and total lipids. The values for esterified cholesterol (as cholesterol oleate) were obtained by multiplying the cholesterol ester values by the factor 1.67.

3. Liver disturbances were excluded by the liver function tests of thymol turbidity; cephalin-cholesterol flocculation; total protein, albumin and globulin ratios.

4. Haematological disturbance was excluded by complete blood count determinations and inflammatory processes by the sedimentation rate.

5. Neither sex, constitutional status, nor age had any effect upon normal blood lipid values.

6. There was marked variation of each lipid fraction percentage of cholesterol (free and ester as oleate), phospholipids, and neutral fats. Addition of these values corresponded to total lipids determined. Cholesterol oleate (esterified) and neutral fats showed the greatest variations.

7. Total cholesterol values are not indicative of total blood lipid elevations.

8. Neutral fat values are independent of high or low lipid phosphorus, phospholipid or cholesterol values. Ratios of phospholipids to cholesterol did not speak for the higher neutral fat percentage. Higher neutral fat percentage values may be found in some normal cases of low phospholipid-cholesterol ratios.

9. The ratio of phospholipid to total cholesterol or vice versa may vary and cannot be considered absolutely suggestive of atherosclerosis or coronary artery disease. High ratio values above 1.00 of phospholipid to cholesterol may be found in older individuals, while ratios of phospholipids to cholesterol below 1.00 may be encountered in the young age group. The ratio of phospholipid to cholesterol may not be a mirror image of the highest blood lipid values. While higher phospholipid cholesterol ratios may be due to lesser cholesterol values rather than higher total blood lipid findings, yet generally the phospholipid values correspond to the higher blood lipid findings.

10. The ratio of cholesterol to phospholipid was found below 1.00 in some normal patients. The ratio of free cholesterol to phospholipid or vice versa was not found to be more constant than the ratio of phospholipid to cholesterol.

CONCLUSIONS

1. Serum lipid fractions as lipid phosphorus, phospholipids, cholesterol, cholesterol as oleate (esterified), neutral fats, and total lipids were defined and determined in normal male and female patients, twenty-two to seventy-two years of age. These serum lipid fractions must be determined to reflect the true blood lipid state.

2. There is a marked variation from the arithmetic mean of the normal serum lipid fractions.

3. Neither total cholesterol alone nor cholesterol and phospholipid determinations reflect high blood lipid changes.

4. The ratio of phospholipid to cholesterol above 1.00 may be encountered in older individuals and below 1.00 in the young age group.

5. One must determine the arithmetic mean values as a base line, because of the variations of the normal serum lipid fraction percentage; the difference in technique; and the variation in the terminology of certain blood lipid constituents.

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SIGMOIDO-RECTAL INTUSSUSCEPTION AND THE UNSTABLE COLON*

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A CONSIDERABLE portion of patients seen in private or clinic practice complain of disorder of colon function. Symptoms have to do mostly with disturbances of the excretory function. These may express themselves by decreased activity of the bowel under sympathetic stimulation which results in dehydrated and less frequent evacuations, i. e., chronic constipation. Chronic non-inflammatory diarrhea, the passage of excess flatus and mucus and constipation alternating with diarrhea are less frequent manifestations of increased secretion and motility of the large bowel acting under the influence of parasympathetic stimulation. The inclusive term, "unstable colon" was introduced by Kantor (1) to apply collectively to these disturbances.

Chronic constipation has been classified as "colonic" and "rectal." Colonic constipation results from inadequacy of purposeful caudad peristalsis in the large bowel; it is most often spastic though the atonic form follows abdominal surgery, pregnancy and severe trauma.

Rectal constipation denotes a failure of the rectum to empty itself. Hurst termed this type of difficult defecation "dyschezia." It most commonly results from the loss of sensitivity to the defecation reflex, the "call of nature." Repeated "holding back" to suit the hurried pattern of contemporary urban life soon results in increased passive tolerance of the normally empty rectum to mechanical distention by the fecal mass.

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Lack of response to distention of the rectum results in failure to "spark" the defecation reflex. This physiologic myoneural response consists of contraction of the diaphragm and abdominal muscles, the longitudinal striae and circular musculature of the rectum, the levators and concomitant relaxation of both anal sphincters. It results in the expulsion of the fecal bolus.

Anorectal lesions such as anal fissures, thrombosed hemorrhoids, cryptitis and papillitis are painful inflammatory lesions which cause reflex spasm of the anal musculature. Rectal stasis is usually present in these conditions because anal relaxation, the final phase of the defecation reflex, does not occur. It is inhibited by the strong reflex contraction of the anal sphincters.

Rectal constipation results from still a third condition, sigmoido-rectal intussusception, a common clinical condition which manifests itself by specific symptoms. Although described seventy years ago by Allingham (2) and repeatedly since then in most textbooks dealing with proctology, (3) the syndrome of sigmoido-rectal intussusception is generally unknown. The reason for this relative obscurity will be discussed presently.

Sigmoido-rectal intussusception is a true intussusception because a redundant, mobile sigmoid loop invaginates into the ampullary portion of the rectum through the rectosigmoid junction. It differs from other types of intussusception in that it rarely becomes strangulated or completely obstructed. On the contrary; the intussusception is intermittent and it reduces itself spontaneously. It has been termed a procidentia of the sigmoid, by which is meant a prolapse of all the coats of the bowel.

The clinical picture resulting from the descent of the sigmoid into the rectum varies widely in individual cases and is often bizarre. It can best be presented by the early description of Harrison Cripps (4) who in 1890 wrote, "the chief symptom is a peculiar difficulty in passing the motions; in other cases in addition to this there is a certain amount of mucoid discharge. The patients generally complain of constipation, for which they have acquired the habit of taking various purgative medicines. They complain that on going to the closet, they have a sensation of wanting to pass a motion without the ability to do so, and that the more they strain, the greater is the difficulty." He further states that, "If, after the bowel has been washed out with an injection, the finger is passed within it, and the patient requested to strain down, folds of loose mucous membrane can be felt crowding down on the finger. By a little manipulation it may be ascertained that these folds are nothing more than the upper and middle part of the rectum invaginated into the lower portion."

Charles Kelsey (5) in 1893 wrote, "The thing most decidedly complained of is a peculiar straining and difficulty in defecation. The patient will say that when he strains the bowel seems to become closed, and that no amount of effort will overcome the obstruction; that to have a passage he has to assume an unnatural position. One of my patients could only relieve himself in the knee-elbow position and the other only when lying down."

In this syndrome characteristically a sense of unsatisfactory and incomplete evacuation remains after defecation. There is a feeling that something remains that should be expelled; consequently the patient sits and strains inordinately. This aggravates the tendency to intussusception. As a result of its frequent descent and recession, congestion and superficial erosion of the mucosa at the apex of the intussusceptum occurs, to result in the discharge of gliary or even bloody mucus. A heavy dragging sensation in the pelvis and in the lumbo-sacral region may be present together with a dull aching pain referred to the perineum and down the thighs.

When the sigmoid prolapses into the ampullary rectum, the lumen of the invaginated bowel is markedly reduced in caliber. Such patients have found, through years of experience, that in order to attain evacuation through the narrowed lumen, the feces of necessity must be semifluid in consistency. Laxation with senna, cascara, prune juice which contains isatin, various salines and mineral oil becomes a daily ritual. The ill effects of prolonged usage of these cathartics are well known. Hyperirritability of the proximal colon with symptoms including flatulence, abdominal distention, crampy abdominal pain and attacks of mucous diarrhea results from overlong use of harsh cathartics. Winkelstein (6) describes gastric symptomatology with complaints including heartburn, belching, vomiting and epigastric pain. These gastric symptoms have been termed "intestinal dyspepsia." They may be direct or reflex effects of colon dysfunction. When direct, the gastric symptoms are caused by distention of the splenic flexture by intestinal gas. Pressure of the distended sigmoid against the posterior wall of the stomach produces the familiar "cascade stomach" which probably gives rise to gastric symptoms.

Reflex gastric symptoms may result through neural pathways stemming from local stimulation of the neural plexuses of Meissner and Auerbach in the anorectum by inflammatory anal lesions such as those previously mentioned. (7). Anal lesions such as cryptitis, abscesses and fissures have been shown to occur much more frequently in individuals who constantly use laxatives. In these persons, the semi-liquid feces readily enter the anal crypts thereby affording access of fecal pathogens to the anal ducts and intramuscular glands, the common source of anal inflammatory disease. (8).

In certain patients with sigmoido-rectal intussusception, the chief complaint appears to be "loose bowels." Typically the patient states that at defecation a thin semi-solid stool is passed. This is followed by a sense of tenesmus and repeated passages of mucoid, sometimes bloody, dejections. If one inquires into the past history, a story of many years of constipation and use of harsh catharsis is elicited. The eventual result of this constant chemical irritation is the development of a granular, hemorrhagic proctosigmoiditis, tenesmus and frequent ineffective evacuations. With severe tenesmus a number of patients suffer post-defecatory proctalgia at times. A history of proctalgia fugax (paroxysmal rectal cramp) can be elicted in about one third of the patients with sigmoido-rectal intussusception.

Mechanically the intussusception depends on three anatomic features: 1) abnormal mobility of the sigmoid due to redundancy and a long mesentery, 2) rigid fixation of the rectosigmoid and rectum by the pelvic and sacral fascia, 3) the narrow caliber of the sigmoid as compared to the voluminous lumen of the rectum. The fascial supports of the rectum reach higher on the posterior wall thus leaving a weak anterior rectal seg-

ment adjacent to the recto-vesicle pouch. This weak anterior rectal wall is vulnerable to increased intraperitoneal pressure so that invagination can and does occur readily in this region.

When symptoms such as recalcitrant constipation, tenesmus, "dragging discomfort" in the pelvis and perineum, bloody mucoid discharge, defecatory proctalgia or proctalgia fugax are elicited, the possibility of sigmoido-rectal intussusception as the cause thereof should be considered.

Sigmoido-rectal intussusception is a common clinical syndrome. We generally fail to diagnose this condition because we ordinarily sigmoidoscope patients in the inverted or knee-shoulder position. In this inverted position the force of gravity acting cephalad, plus atmospheric pressure entering through the scope, displaces the prolapsed sigmoid into its normal anatomical position in the proximal pelvis. However, if this patient is examined in the Sim's position the procidentia can be readily demonstrated. The instrument is again passed full length into the sigmoid of the now recumbent patient. Air insufflation facilitates this maneuver by dilating the lumen thereby increasing the range of visibility. The scope is now slowly withdrawn and the air is allowed to escape by removing the air sealing window. When the scope reaches the ampullary rectum and the distal aspect of the rectosigmoidal junction is visualized the patient is asked to "strain down." The sigmoid is seen to prolapse through the rectosigmoid usually appearing first at the anterior aspect of the rectum. With further withdrawal of the instrument and continued straining by the patient, the apex of the intussusceptum frequently can be seen to descend to the sphincteric rectum. If digital examination is now performed the apex of the sigmoid intussusceptum is palpable. This firm knuckle of sigmoid feels soft, slippery and sausage-like. Finger pressure thereon elicits rectal pain.

Strangulation, though uncommon, may occur. Monsarrat (9) of Liverpool operated on a 46 year old male for acute, low intestinal obstruction. He found the sigmoid invaginated into the rectum. The strangulated loop of sigmoid was reduced by tradition from above and fixed by sutures to the pelvic brim. He reported three other cases which were similar. I have two cases in which the sigmoid was incarcerated into the rectum at the rectosigmoidal junction. Severe obstipation was present and on examination a velvety-soft, edematous, tender, injected segment of intestine with an obliterated lumen, was palpated digitally and visualized endoscopically in the rectal ampulla. This mass of gut was firmly incarcerated and could not be reduced by manipulation from below. The patients were treated expectantly. Fortunately, edema of the incarcerated sigmoid subsided, so that manual reduction was accomplished after several days. Subsequent examinations on several occasions demonstrated sigmoido-rectal procidentia. Incarceration has not recurred.

Many attempts have been made to demonstrate the sigmoidal intussusceptum roentgenographically. Despite the use of various positions, barium mixtures of varying viscosity, consistency, and density, alone or combined with air insufflation, a satisfactory technic has not been developed.

TREATMENT

The constitutional nature of sigmoido-rectal intussusception makes successful treatment difficult. The prolonged constipation and the abuse the colon has been subjected to by previously ill advised treatment by harsh cathartics presents a therapeutic challenge well known to all. Added to this is the fact that many patients are women in or past the climacteric, some with personality difficulties and others with definite psychoneurotic traits.

Relief of anxiety in such patients (many of whom have cancer phobia) can be attained by patiently and simply explaining to the patient the mechanics of the disturbance at the conclusion of a very complete examination which must include a barium enema and sigmoidoscopy. Harsh cathartics are banned. A high protein, high vitamin, low roughage diet is ordered. Hydrophilic preparations, (psyllium, karaya, methylcellulose, etc.) are administered in sufficient and frequent dosage so as to produce a firm, slippery stool of large size. This firm, bulky stool mass fills and dilates the distal sigmoid. It will slip through the rectosigmoidal junction readily and easily to completely fill the ampulla of the rectum, thereby forestalling sigmoidal invagination. Patients are cautioned against straining unduly at stool. Should no bowel action result for two days, a plain warm water enema, no more than a pint at a time, best taken before retiring is advised. This must be administered with the patient supine and with the knees drawn up on the abdomen. In this position, the hydrostatic pressure will mechanically reduce the "plug-like" sigmoidal intussusceptum which prevents the fecal mass from passing into the rectum. Mild sedation, antispasmodics, the hormones (estrogen, testosterone, thyroid) are necessary adjuvants of treatment utilized when indicated by the general medical condition of the patient.

It should be emphasized that anorectal inflammatory lesions such as chronic fissures, cryptitis, papillitis and pectinosis are frequently present. These must be eradicated by anoplastic surgery thereby eliminating neuromuscular reflex effects so frequently a causative factor resulting in a hyperirritable, spastic colon. (7).

Constant reassurance, skillful expectant management of symptomatic episodes and considerable patience on the part of the physician should result in satisfactory therapeutic results. In severe intractable cases, resection of the redundant sigmoid and obliteration of the anterior rectal peritoneal hernia by plastic obliteration of the pouch of Douglas (Moschkowitz's operation) might be considered as a radical means of attaining cure. One such symptomatically intractable case occurring in a physician was treated surgically with success. (9).

SUMMARY

1. Although repeatedly described for over seventy years, the syndrome resulting from sigmoido-rectal intussusception is generally obscure.

2. Typical symptoms include extreme chronic constipation, defecation characterized by a sense of incomplete evacuation, tenesmus, occasionally bloody mucoid dejections, "dragging discomfort" in the pelvis and perineum, defecatory proctalgia and occasionally, proctalgia fugax.

3. We frequently fail to diagnose sigmoido-rectal procidentia because we generally sigmoidoscope patients in the inverted knee-shoulder position in which the intussusceptum spontaneously reduces itself. The lesion is easily demonstrated if the patient is re-examined in the recumbent Sim's position.

4. The unstable colon syndrome is frequently a sequel of sigmoid-rectal intussusception induced probably by prolonged use of harsh cathartics.

5. Treatment is generally satisfactory but requires patience, tact and persistence on the part of the physician as well as faithful cooperation on the part of the patient.

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PRIMAL AFFECTIONS OF APPENDICES EPIPLOICAE

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THUS FAR, MOST articles pertaining to disease of the appendices epiploicae have stressed the infrequency of this condition. Such a view seems justified by the scarcity of cases on record, but a revaluation of the literature substantiates the view of Daniel C. Patterson (1)—". . . that disease of the appendices is more frequent than we realize, and the possibility of its presence should always be borne in mind . . ."

While I have been able to find, up to this writing, only 99 (2, 3, 4, 5, 6) case reports of affections which originated in the appendices epiploicae and gave rise to symptoms justifying operation, it is of great significance that 15 (2, 3, 4, 5) of these were published in a 12 month period (April 1949 to April 1950). Cases in which appendices became incarcerated in hernial sacs, cases in which adherence of appendices to adjacent structures caused intestinal obstruction, and cases in which primary disease of appendices was found at operation for other disease processes or at necropsy, are not included. There is little doubt, moreover, that many operated cases are not reported. After Patterson (1) had read his paper, "Appendices Epiploicae," presenting 3 new cases, at a meeting of the New England Surgical Society in 1933, 3 surgeons in the audience stated that they had operated on one similar case each. I have been unable to discover that any of the latter were reported. Of further importance in evaluation of the published statistics is the fact that a preoperative diagnosis of disease of an appendix epiploica cannot be substantiated without operation. If inflammation of an appendage resolves spontaneously or if a torsion rights itself, the symptoms subside and the patient recovers, but the diagnosis remains unproven.

Although most published reports are of single cases, there have been some in which a small series was presented. Of the latter, the earlier groups show a much lower incidence. Only 9 cases were observed at the Mayo Clinic (7) from 1920 to 1942, and Mabrey (6) reporting one personal case in 1940 stated that he had been able to find only 5 cases in the records of the Massachusetts General Hospital. On the other hand, Ladin (5) reporting from the relatively small Lebanon Hospital, found 4 cases in a decade (1938 to 1948), and Marinis and Cheek (4) reported finding 6 cases at the somewhat larger Baylor Hospital during virtually the same period.

I have 5 personally operated cases to add to those on record. They were operated on in the years from 1925 to 1948. During the 10 year period covered by Marinis and Cheek's (4) 6 cases, 2766 patients were operated on at the Baylor Hospital for acute appendicitis, or one operation for epiploic appendage to 461 for appendicitis. Using the same yard stick for my cases, the ratio was 1 to 465—5 operations for epiploic appendage to 2324 for appendicitis.

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REPORT OF CASES

Case 1. K. G., a 31-year-old male, was seen at my office on January 30, 1925. He complained of having had intermittent attacks of abdominal pain over a period of one and one-half years. The pain was localized on the right side of the abdomen between ribs and ilium. There were no gastro-intestinal symptoms except for a sensation of "gas" after eating.

Abdominal examination disclosed no tender areas and no masses. Roentgenograms were taken, and the report was as follows: "Just near the right posterior inferior spine of the ilium there is an irregular, dense, apparently calcified shadow, about 3 x 4 cm. in diameter." Cystoscopic, pyelographic and urine examinations were negative.

Pre-operative diagnosis: Calcified mesenteric lymph node.

Operation was performed at the Chelsea Memorial Hospital on February 13, 1925. Attached to the cecum by a long, narrow pedicle was a calcified mass conforming in size and shape to the roentgenogram description. The mass was excised. There were no other abnormal findings. The convalescence was uneventful. When seen 24 years later, the patient stated there had been no recurrence of symptoms.

Diagnosis: Calcified appendix epiploica.

Case 2. P. K., a 32-year-old male, was seen at his home on March 8, 1935. His complaint was abdominal pain of a week's duration. The pain was to the right of the umbilicus, was not severe, and was described as being more like a "gas" pain; but, at times, when the patient was walking, the pain caused him to double up. There was no nausea or vomiting.

Abdominal examination revealed a moderately tender area about the size of a silver dollar to the right of the umbilicus. There was also slight distention. No masses could be felt. The temperature, white blood cell count and urine examination disclosed no deviation from the normal.

Because symptoms persisted, the patient was admitted to the Beth Israel Hospital two days later. A gastro-intestinal

roentgenologic examination, including a barium enema, was reported as negative; the appendix was not visualized. The patient was kept under observation for four days, the pain and tenderness remained unchanged.

Pre-operative diagnosis: ? Appendicitis. ? Torsion of appendix epiploica.

Operation was performed on March 14, 1935. Coming off from the ascending colon was a twisted, ecchymosed, epiploic appendage, which was adherent to the omentum. The appendage was excised. Abdominal findings were otherwise negative. The convalescence was uneventful.

Diagnosis: Torsion of appendix epiploica.

Case 3. E. C., a 45-year-old, single, female, was seen at the Forest Hills Hospital on October 2, 1933. Her complaint was abdominal pain of two days duration. The pain was in the right lower quadrant, and was aggravated by motion. She had a sensation of increased pressure as if due to much "gas" in her intestines. One week before admission she had had a similar attack; but the pain, on the left side of the abdomen, was not as severe, and disappeared at the end of two days. A month previously she had had an attack of pain which she could not localize and which lasted but a few minutes. At no time was there nausea or vomiting.

Abdominal examination disclosed tenderness and resistance in the right lower quadrant. No masses could be felt. The pelvic examination was negative. The temperature was normal, the white blood cell count was 13,000, and the urine examination disclosed no abnormal findings.

Pre-operative diagnosis: Acute appendicitis.

Operation was done promptly. Coming off from the ascending colon was a twisted and gangrenous epiploic appendix. This was excised. Abdominal findings were otherwise negative. The convalescence was uneventful.

Diagnosis: Torsion and infarction of appendix epiploica.

Case 4. D. F., a 58-year-old, obese, married, female, was seen at the Malden Hospital on April 28, 1937. She complained of generalized abdominal pain of two days duration. Roentgenograms taken two years previously revealed diverticulosis of the sigmoid.

Abdominal examination disclosed indefinite tenderness and resistance at the left lower quadrant. No masses could be felt. The pelvic examination was negative. Temperature was 100° F., and the white blood cell count was 16,000; the urine was negative.

The patient was kept under observation for three days, with no subsidence in symptoms or physical findings.

Pre-operative diagnosis: Acute diverticulitis of sigmoid.

Operation was done on May 1, 1937. Low on the sigmoid was an edematous epiploic appendage, flecked with fibrin. The appendage was excised. The abdominal findings, other than for the diverticulosis, were negative. The convalescence was uneventful.

Diagnosis: Acute inflammation of appendix epiploica.

Case 5. J. C. B., a 26-year-old male, was seen at the New England Hospital for Women and Children on August 17, 1948, because of abdominal pain of three days duration. The pain came on gradually and increased in severity. It was made worse by deep breathing. The pain was so severe on admission that a hypodermic injection of morphine was given. There was no nausea and no vomiting.

Abdominal examination disclosed considerable tenderness, but no spasm, in the right upper quadrant. No masses could be felt. Temperature was 100° F., and white blood cell count 16,300; urine was negative.

A gastro-intestinal roentgenologic examination was reported as negative. During the course of four days observation, the temperature continued to be elevated, the pain persisted, was severe enough to require repeated hypodermic injections of sedatives, and the abdominal findings remained unchanged.

Pre-operative diagnosis: Acute cholecystitis.

Operation was done on August 21, 1948. Gall bladder appeared normal in every respect. Coming down from the region of the hepatic flexure was a twisted and gangrenous epiploic appendage. This was excised. The abdominal findings were otherwise negative. The convalescence was uneventful.

Diagnosis: Torsion and infarction of epiploic appendix.

COMMENT

From an anatomic-physiologic view-point there is no reason why epiploic appendices should be immune to pathologic change. They are small pouches of peritoneum filled with fat, and are attached by pedicles along the colon down to the rectum. They are usually ranged in two rows, but one or three rows are frequently seen. An adult has about 100 of these appendices (8), which may vary in length from 0.5 cm. to 5.0 cm. They have been described as being up to 15 cm. long (1), and they are motile. Robinson (10) demonstrated experimentally that the introduction of fluids into the colon causes rhythmic to-and-fro motion of the appendices. In intraperitoneal inflammation they appear to aid in forming a barrier against the spread of infection. One appendage was found wrapped around a perforated appendix (8). The number, size, shape, location and motility of appendices make them vulnerable to inflammation and torsion.

Since the appendices are contiguous to the bowel, it is possible for them to be invaded by micro-organisms from the colon. Colon bacilli have been isolated from removed specimens (11). Appendices may undergo inflammatory change because of their intimate anatomical relationship to diverticula. A diverticulum may communicate directly with an appendage and may become involved by diverticulitis; conceivably this may go on to abscess formation and may be the cause of some of the unexplained cases of peritonitis. Inflamed appendices may also become attached to adjacent structures and cause intestinal obstruction.

Torsion of appendices can be sudden or gradual. Sudden torsion is sometimes accompanied by congestion with resulting necrosis and complete gangrene. Gradual torsion may eventually interfere with blood supply and be followed by saponification and calcification as in Case 1. With complete atrophy of the pedicle, the appendage may separate from its base. It then becomes a loose body, lying free or surrounded by omental adhesions (10).

There is nothing distinctive about the symptoms of disease of the appendices epiploicae except that there is always pain. With sudden torsion the pain may be quite intense. Sometimes, but not usually, there is nausea or vomiting. At first the pain is generalized; later localization takes place, the site varying according to the location of the appendage. With gradual torsion or inflammation the pain is relatively mild; often there is a history of pain extending over a period of several days. Three of my patients described their discomfort as if due to distention by "gas." If an appendage becomes adherent to an adjacent viscus or intestine, the symptoms may be those of intestinal obstruction.

On physical examination, unless complications are present, these patients do not appear to be particularly ill. With sudden torsion, at least in the beginning, there is no fever. Later, with infarction, the temperature may be moderately elevated (up to 100° F. in 5 cases reported), and the leucocyte count may be increased. In about one-half of the cases on record there was a varying amount of rigidity of the abdominal wall; in others, there was only moderate tenderness. With gradual torsion, all physical findings are essentially negative. With inflammation, as in Case 4, there is moderate elevation in temperature and white blood cell count,

and, on abdominal examination, tenderness and resistance. Should abscess formation take place, all these findings will be intensified. With a complicating obstruction there will be distention and other findings of this condition.

Diagnosis of disease of an appendix epiploica can be made only by excluding all other possibilities. There are no laboratory findings to help identify this condition. If roentgenograms are taken in cases of gradual torsion, the finding of calcification will furnish the clue to the correct diagnosis. The diagnosis of torsion or inflammation is usually mistaken for appendicitis, cholecystitis, torsion of ovarian cyst, mesenteric adenitis, Meckel's diverticulum, diverticulitis of colon, ruptured graafian follicle, renal calculus or intestinal obstruction. Fiske (11) reported that Wayne Babcock made a correct preoperative diagnosis before operation in one case, and it was considered in Case 2.

If the symptoms are mild, observation is indicated. Spontaneous resolution may take place; inflammation may subside, or a torsion may untwist itself. In one of the Massachusetts General Hospital cases (6), an inflamed appendage was not removed because of its inaccessibility; symptoms subsided in 10 days. If the pain persists or increases, operation is warranted. For torsion, simple excision of the appendage is sufficient. If there is inflammation, the possibility that a diverticulum may be present should be kept in mind. In such cases, after removal of the appendage, the base should be carefully approximated and covered with peritoneum.

If no complications are present, the convalescence should be uneventful. Should there be infection or a complicating intestinal obstruction, then obviously there will be an increase in morbidity and mortality. Of the cases on record (6), there were 4 deaths due directly to disease of an appendix epiploica. One was due to paralytic ileus, another to intestinal obstruction, and two to generalized peritonitis—one following intestinal obstruction and the other drainage of an abscess.

CONCLUSIONS

1. The number, shape, size, location and function of appendices epiploicae make them susceptible to torsion and inflammation.

2. The paucity of case reports should not be accepted as indicative of the incidence of primal disease. The only cases published have been those that came to operation. Cases in which a torsion righted itself or inflammation subsided may very likely greatly outnumber those coming to operation. However, without operation the diagnosis can not be substantiated.

3. Based on the series at the Baylor Hospital and on the above reported cases, the incidence of appendices coming to operation, as compared with the incidence of patients requiring an appendectomy, is about 1:463.

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THE TREATMENT OF OBESITY

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OBESITY IN OUR civilization has become a major health problem. Public health workers respect its adverse effect on longevity. Nevertheless, its importance is not as sufficiently emphasized as it deserves to be. The lay public and even many physicians tend to look at the obese as jolly, "well-nourished," comical characters who seem to carry their abnormality rather harmlessly and frequently by choice.

It is this distorted image of the obese which contributes to the neglect of a serious situation by both the patient and the physician. The obese person, contrary to the common impression, is more likely to be a less contented soul than his thinner brother. Either consciously or subconsciously, he recognizes that his adiposity is a fit subject for ridicule, and is generally a social handicap. The development and continued existence of obesity is related to patterns of resentment, frustration, and feelings of inferiority. It is frequently difficult to determine the cause-and-effect relationship of obesity to psychoneurotic disturbances. Nevertheless, the re-establishment of a normal physiognomy may constitute a major contribution toward a favorable psychological adjustment pattern, and vice versa.

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It is universally recognized that obese people have a shorter life expectancy (1, 2, 3). They are more likely to become hypertensive (4). Their muscles, including cardiac muscle, must perform a greater amount of work to achieve a unit of activity. Cardiac patients are more likely to go into failure if they are obese (5). Cardiovascular disturbances occur more frequently and may be responsible for the increased incidence of renal disease in the obese (4). Menstrual function and fer-

tility are often disturbed (6). Diabetes is more likely to appear and more likely to increase in severity if the patient becomes overweight (7).

Gall bladder disease, with all its accompanying digestive disturbances, is apparently more common in the fat person. Structural defects such as postural abnormalities with related ligamentous and joint strains, may contribute to the incidence and severity of sacroiliac and other arthritic pains. Hernias, varicose veins and hemorrhoids are more common (4). Infectious processes frequently are more difficult to clear in the obese, and, when surgery is necessary, there are added problems to the patient, surgeon and internist.

All these facts should lead the physician to exert every effort to understand and control the problem of the obese patient. Unfortunately, the need for a clearly thought-out approach to the problem has not been given sufficient stress. Frequently, the patient is casually told to eat less, or that he is "fat by nature," and little guidance is given to him. A slap on the back with a vague admonition about "fattening foods" is sometimes the only treatment offered. This is seldom adequate. A specific, well-planned program must be presented to assure the patient's understanding and cooperation. Without patient cooperation, the physician's best efforts are doomed to fail.

The importance of giving the patient some insight into the cause and dangers of his obesity should not be overlooked. The fat person should be made to understand that in spite of all other factors, including his glands, his heredity and his psyche, the development of obesity results from a positive energy balance, i.e. more food is being taken in than is being burned up. In those instances involving decreased metabolism due to endocrine dysfunction, the deposition of fat is incidental and likely to distribute in a manner different from that seen in common exogenous obesity. Other signs and symptoms will usually help establish the role of disturbed internal secretions in the small percentage of people who suffer from these conditions. But regardless of what other factors are operating, obesity is still the result of excessive food intake. The habit of over-eating, in most instances, is a response to an unsatisfactory life situation or personality disturbance. Every age group, from the pre-pubic through the postclimacteric, is subject to insecurities and maladjustments which may lead to excessive food ingestion. In the pre-pubic group, food getting represents one of the earliest instincts, which is frequently more than satisfied by parents who think the fat child is a healthy child. Later, some parents overcome a child's disturbing manifestations of displeasure by stuffing him with food as a substitute. Thus a child's obesity is frequently a reflection of his parents' maladjustments.

The adolescent is subject to obviously difficult adjustments. Difficulties in coping with these problems may result in eating as a substitute for adequate adjustment to the changing life situation. This may initiate a life-long vicious cycle: over-eating as a compensation for inferiority feelings, and feelings of inferiority being nourished by an ugly obesity.

During the adult phase, and later in the menopause, food ingestion habits may similarly develop as a compensation for maladjustment to the problems of these periods. Hence, from the physical standpoint, the development of marked obesity is indeed serious, since it leads to a shorter life duration and greater suffering from the conditions listed above.

PROGRAM OF TREATMENT

The physician who undertakes the treatment of obesity cannot hope to regularly reestablish a favorable relationship between the patient and his environment. This, of course, would be the ideal way to avoid the habitual ingestion of abnormal amounts of food. However, supplementary means of reducing weight must frequently be employed. Obtaining a more favorable caloric balance by increasing the energy consumption is impractical. Experiments indicate that walking exercise alone requires for the average person a walk of 10 extra miles per day for one week to lose 2 pounds of adipose tissue (8). Such exercise frequently stimulates the appetite to a degree up to and beyond the calories consumed. The use of medication to increase basal metabolic rate is a dangerous procedure and is not generally recommended. Such drugs are reserved for those instances where examination indicates a real need for increasing the metabolic rate of resting tissues. Consequently the physician must concentrate on curbing the appetite and the control of eating habits. To accomplish this the following program has been developed and employed in the cases reported in this paper.

1. Gain the confidence and maintain control of the patient. The patient should be convinced of the necessity for losing weight. The health hazard of obesity is explained in detail. On successive visits the inter-relationship of obesity and maladjustment is gradually made clear to the patient. This superficial form of psychotherapy is of fundamental importance and is coupled with encouragement concerning the ultimate success of therapy. This portion of the program will require weekly visits. It is most helpful to demonstrate some success to the patient, such as some loss in weight, drop in blood pressure, or other improvements in obesity-related disturbances during the course of treatment.

2. Insist on the development of a satisfactory dietary habit. At first this must be done by instructing the patient specifically on which items he may or may not eat. Between-meal nibbling is strictly forbidden or confined to raw cellulose vegetables of low caloric value. Once again frequent visits are essential to remind the patient of the rules of diet. A recommended diet sheet is reproduced below. It was also designed to take into account several important factors learned by experience other than simple reduction of caloric intake. These factors are discussed below.

a.) Include adequate bulk and essential dietary factors. Occasionally problem cases are hospitalized and given near-starvation diets in a desperate effort to reduce weight. Frequently, this results only in severe weakness. Even when some weight loss is achieved, it is promptly regained after discharge from the hospital. Administration of known vitamin substances in an adequate quantity is an essential supplement to any limited diet used over prolonged periods.* However, one must recognize that the last word concerning nutrition has not yet been said. Empirical observations indicate that adequate amounts of natural food substances must be provided in any long range program in spite of pure vitamin supplements. Consequently the necessary re-

duction in caloric intake must be accomplished not by "across the board" cuts in the patient's intake, but by changing the nature of that intake as indicated.

b.) Markedly reduce the intake of purified carbohydrates. *All* bread, sugar, cakes, etc. must be completely eliminated in favor of the carbohydrate-containing bulk vegetables. It has been noted that diabetic patients use less insulin and are better controlled on a diet with a given amount of carbohydrate in a natural vegetable form than if fed a diet with the same carbohydrate content in a purified form. Similarly, experience has taught that even small amounts of refined starches or sugars may markedly interfere with the efficacy of a reducing diet. Only after fall in weight to the desired level has been achieved may one or another particularly desired carbohydrate food be added and its effects carefully observed before the addition is permanently allowed.

c.) Include liberal portions of high protein food. A large negative nitrogen balance is undesirable during attempts at weight loss. It is the fatty depots which one is attempting to reduce. Proteins are essential to good nutrition, and in some instances, obese people are actually nutritionally deficient, and may be suffering from inadequate protein intake. The specific dynamic action and other characteristics of protein metabolism are such that fat deposition does not result from high caloric protein diets which are low in carbohydrate and fat. Consequently, protein foods may be given liberally.

d.) Educate the patient. The object of therapy is to teach the patient new eating habits. The patient's loss of weight indicates whether or not he is learning his lesson. The period of treatment is determined by how quickly the new habits of eating and living are learned. To help eliminate certain undesirable taste habits, some prohibitions are instituted which of themselves are not fat producing, i. e. coffee is permitted in limited quantity and not only is cream and sugar forbidden, but other sweetening agents such as saccharin are not allowed. Excessive salt and pickled foods are also prohibited. Only when the patient has developed a dietary habit which maintains his optimum weight, is he ready for discharge. He should therefore be told that he is not undergoing treatment for a set time interval, but rather is being subjected to a re-education program, the duration of which will depend upon his capacity and desire to learn. The optimum weight is judged as that at which the patient feels and looks best, without regard to any arbitrary tables.

3. Medication: It is frequently advisable to supplement these measures with medications of two types:

a.) Appetite-curbing drugs. There is now abundant evidence that the amphetamine type of appetite-curbing medication is an effective aid in the treatment of the obese (9, 10, 11) and is much more effective than thyroid medication in exogenous obesity (6).

The use of Norodin, N. N. R.* (methamphetamine) 5 or 10 mg. 2 or 3 times a day, has been found to be effective (12, 13) and was used as the appetite-curbing drug of choice in the obese patients reported in this study. The medication is begun in the smaller dosage. It is taken in the morning and afternoon and avoided before bedtime. Weekly checks of the pulse rate, blood pressure, and symptoms of agitation, are conducted while this drug is being administered, even though side effects rarely appear to any serious degree.

b.) Medication to relieve symptoms of complicating factors: Where biliary disturbances were part of the picture, a combination of ketocholanic acids and methamphetamine (Ganone, Endo) were employed. Neglect of complicating conditions may threaten the success of the entire program.

MATERIAL

This report is an analysis of 74 cases who followed prescribed therapy and reported for examination and interview weekly or bi-weekly. Initial examination included a complete history with special reference to the development and nature of the personality picture. Complete physical examination was performed with the history in mind in an attempt to distinguish symptoms of organic origin from those which were primarily psychogenic.

There were 64 women and 10 men in the group. 48 were married; their ages ranged from 16 to 84, averaging 35.3 years. 35 were housewives, and 12 only were engaged in occupations requiring physical exertion. 25 had previously attempted weight reduction under medical guidance without success. Of the 74 patients, 38 complained of a variety of symptoms which were judged to have a major psychogenic component. Complicating disturbances of organic origin included 15 patients with dyspnea, seven with other cardiac complaints, 9 with biliary disturbances, 5 with arthritis, and 4 with evidence of true hypothyroidism. 24 patients had blood pressure readings of over 150 systolic or 100 diastolic. All subjects were considerably overweight. 58 of the 74 weighed over 200 lbs. on the first office visit.

TABLE I

Time of examination	Average weight lbs.	Number of patients over 200 lbs.	Number of hypertensive* patients
Initial	208.7	58	24
Final	146.3	4	5

*Systolic pressure over 150 or diastolic over 100 mm. Hg.

RESULTS

Therapy as outlined above was continued until adequate weight loss was achieved. The average weight of these subjects at time of discharge was 62.4 lbs. less than at the time of initial visit. (Table I). Of the 24 patients with blood pressure readings exceeding 150 systolic or 100 diastolic at the initial examination, only 5 persisted with tensions above these limits at the conclusion of therapy, and all of these 5 also demonstrated reductions to levels below the initial values. Improvement in other complicating factors, both organic and psychogenic, could not be analyzed in objective numerical terms, but the regularity of improvement in these factors with therapy was none the less striking.

DISCUSSION

It is apparent from the data reported that the problem of obesity can be successfully met in the physician's office. The reported experiences suggest that once the magnitude of the problem is sufficiently recognized and physicians are prepared to spend the time and effort necessary for the proper management of obesity, satisfactory results can be achieved. The importance of close supervision and frequent observation in controlling the related emotional factors is

frequently overlooked. There can be no blanket mimeographed routine of medication and diet which alone will suffice for the treatment of all obese patients. Where appetite is excessive, it must frequently be curbed by medication. Our experience with Norodin, N.N.R. for this purpose has been gratifying. Ultimately the curbing of appetite should be achieved by the newly formed pattern of the patient's eating habits. Complicating symptoms must also be treated individually, where and when they are noted. It should thus be possible to eliminate much of the hopeless attitude which frequently accompanies the treatment of the obese.

When weight has been reduced to the desired level, the frequency of office visits may be reduced. However, the patient must be cautioned to continue his vigilance. It is a good rule to instruct the patient at the time of discharge that he must watch his weight, and return to the office if he should regain more than 5 pounds above an optimum weight. In this manner the physician may make a major contribution to the practice of preventive medicine among his private patients.

*Since this report was submitted, we have found it advantageous to use a water-soluble polyvitamin combination (Vifort Capsules) in order to reduce exogenous fats further. Each provides vitamin A, 5000 units; vitamin D, 500 units; mixed tocopherols, 2 mg.; thiamine mononitrate, 3 mg.; riboflavin soluble, 2 mg.; nicotinamide, 20 mg.; panthenol, 5 mg.; pyridoxine, 0.3 mg., and ascorbic acid, 60 mg. all in water-soluble form.

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ABSTRACTS ON NUTRITION

BETHELL, F. H., SWENDSEID, M. E., MILLER, S. AND CINTRON-RIVERA, A. A.: *Cobalamin (vitamin B_{12}) and the intrinsic factor of Castle.* Ann. Int. Med., 35, 3, Sept. 1951, 518-28.

The authors suggest the generic name "cobalamin" for the various forms of vitamin B_{12}, viz., B_{12} and B_{12b}. All the various forms appear to possess the same degree of hemopoietic activity. Solutions of vitamin B_{12} or B_{12b} by injection are effective substitutes for liver extract in pernicious anemia. The authors present two cases, one of which, particularly, appears to be a megaloblastic (macrocytic) anemia due to lack of B_{12} in the diet, who responded to the oral administration of only 5 micrograms daily without the addition of gastric or duodenal mucosa. This patient was an alcoholic who had used an inadequate diet. In one case of pernicious anemia they found that a heated trypsin digest of intrinsic factor—cobalamin complex was hematologically successful. In one case of megaloblastic anemia due to faulty intestinal absorption, it was found that folic acid was necessary in conjunction with "cobalamin."

STAMLER, J. AND KATZ, L. N.: *The effect of pancreatectomy on lipemia, tissue lipidosis and atherogenesis.* Circulation IV, 2, Aug. 1951, 255-261.

Pancreatectomized chicks exhibit an excessive hypercholesterolemia when fed a diet containing cholesterol plus cottonseed oil. This inordinate hypercholesterolemia is accompanied by intensified atherogenesis, compared with unoperated controls on the same diet.

Neutral fat is essential for these excessive cholesterolemic and atherogenic responses, since they are absent in depancreatized cockerels fed mash supplemented only with cholesterol. Plain mash-fed pancreatectomized cockerels exhibit intensified spontaneous atherogenesis, although they have a normal plasma lipid and glucose levels.

STAMLER, J., PICK. R. AND KATZ, L. N.: *Effects of Desoxycorticosterone acetate on cholesterolemia, blood pressure and atherogenesis in chicks.* Circulation, IV, 2, Aug. 1951, 262-269.

Giving desoxycorticosterone acetate over periods up to 15 weeks induces cardiac hypertrophy, polydypsia, adrenal hypoplasia, decreased comb size indexes and moderate nephrosclerosis in cockerels. A definite, but not severe, rise in blood pressure occurs. The polydypsia and hyperpiesis induced by DCA are increased by the addition of 1 percent sodium chloride to the mash; neither supervene in DCA-treated chicks on a low sodium diet. In cockerels given a mildly atherogenic supplement of cholesterol in their mash (0.25 percent), concomitant DCA administration increases the incidence and severity of atherosclerosis. Further work is needed, especially to determine the effects of cortisone on lipid metabolism and atherosclerosis.

BABA, H.: *Relation between mottled teeth, the amount of fluorine in drinking water and inferior physical constitution in and around Dogo-hot-spring District, Ehime Prefecture, Shikoku Region.* Shikoku Acta Med., 1, 2, Dec. 1950, 78-83.

In an extensive examination of the amount of fluorine in drinking water in the designated district, it was found that well water used by 32 children with mottled teeth averaged 3.6 parts per million while the water used by 8 children without mottled teeth contained, on the average, 0.25 p.p.m. At Matsuhama there were no mottled teeth in those children using well water devoid of fluorine but mottling was found among those using "service" water containing 1.8 p.p.m. At Yuyama the boys with mottled teeth are shorter in height than those without mottling, and apparently this is due to fluorine.

KURODA, K.: *On the transition of the nutritional state of the Japanese during the war from the standpoint of the blood water content.* Shikuku Acta Med. Vol. 1, No. 1, Oct. 1950, 13-24.

The author employs a micro-method of comparing the fresh weight with the dried weight of blood, the difference representing the water content. He made 4023 observations on men and 438 on women between 1941 and 1945. During the latter period of the war, nutritional hydremia was observed in a considerable portion of the Japanese and apparently occurred before clinical signs of malnutrition appeared. This hydremia was higher in women than in men, and higher in the extremes of age, and higher also in urban than in rural inhabitants. The changes in hydremia closely corresponded with the food supply during the war.

GEOFF, A. E. ENGELHART, H. T. AND SKELTON, J. M.: *Clinical evaluation of NPH-50 insulin in the management of diabetes mellitus.* Texas State J. Med., 47, 8, Aug. 1951, 547-552.

The authors found that NPH insulin produced a remarkably stable blood sugar level, so that its use in "unstable" diabetes seems advisable. The peak of its activity appears 8 or 9 hours after subcutaneous injection. It is better than protamine zinc insulin in patients needing more than 30 units daily. Some patients, of course, will require mixtures of NPH and regular insulin for their proper management.

MAZUMDAR, D. C., AND MUKHERJI, K. L.: *Nutritional edema leading to spontaneous hypoglycemia.* J. Indian Med. Assoc., XX, 10, July 1951, 361-365.

In 3 cases of nutritional edema, each with anemia, the phenomenon of spontaneous hypoglycemia was encountered. It was corrected by giving glucose. One of the cases *may* have been insuloma. In the third case who was very anemic, the blood sugar went as low as 17 mg. percent. On doing a glucose tolerance test on this patient, there was a steady rise in the blood glucose for 7 hours till it reached about 200 mg. percent. This was unexplainable. Later he took a severe diarrhea and died.

EDITORIALS

JAPAN'S NATIONAL INSTITUTE OF HEALTH

The Japanese National Institute of Health was created May 21, 1947 under the jurisdiction of the Ministry of Welfare, whose duties are the improvement of the social welfare level, social security and public health. The Institute may conduct and coordinate research projects, assay and control biological preparations, and antibiotic preparations. It is also the "national diagnostic center," and is further responsible for the technical activities of public health laboratories of all types. The Institute has been selected as the official channel for the international interchange of information, and was selected as one of the regional influenza centers by W. H. O. Branch institutes in Hiroshima and Nagasaki are cooperating with the Atomic Bomb Casualty Commission of the National Research Council of the U. S. A. in joint investigations on the effects of atomic explosions. The research results of the Institute are either published in periodicals or issued as directives. The Japanese Medical Journal is a publication of the Institute. This centralization of medical responsibility is admirable and combined with Japanese industry and ingenuity, augurs well for the future of Japanese medical research.

SEDATIVES IN GASTROENTEROLOGY

It is a truism that most cases of functional gastrointestinal upset improve more rapidly if a sedative is used at least temporarily. As everyone knows, however, there exists at present no perfect sedative. Few gastroenterologists today employ bromides because of the ease with which bromism frequently develops. Phenobarbital, at least in small doses, works fairly well in the majority of people but it often produces serious mental depression in susceptible persons and there is the occasional case of severe dermatitis resulting from its continued use. Chloral hydrate might be excellent except that it may be definitely habit-forming. Many of the fast-acting sedatives, while harmless, are less valuable than phenobarbital since their action is evanescent. For these and other reasons the profession has long desired a more perfect sedative, combining the advantages without the disadvantages of those now in general use. Possibly in time such a sedative will be forthcoming. At the moment it might be well for the pharmaceutical houses to investigate the lithium salts more fully. Recently Noack and Trautner (1) have shown that *mania* can be safely controlled by lithium carbonate or lithium citrate, and it is reasonable to suppose that much smaller doses than they used would suffice for ordinary sedation and would naturally be free of the dangers attending the use of large doses. Perhaps lithium owes its sedative effect to a displacement of sodium chloride but this point is not entirely settled.

(1) Noack, C. H. and Trautner, E. M. The lithium treatment of maniacal psychosis. Med. J. Australia, Aug. 18, 1951, 219-222.

BOOK REVIEWS

TEXT BOOK OF LAPAROSCOPY AND GASTROSCOPY (LEITFADEN DER LAPAROSCLOPIE UND GASTROSKOPIE). Kalk, H., Bruehl W., Burgmann, W. 158 pages, 82 mostly colored illustrations. Thieme, Stuttgart, Germany, 1951. $6.50.

This book is an introduction to laparoscopy and gastroscopy. Kalk, who has a tremendous experience in the former field, describes very thoroughly the preparations and technique of this type of examination. He emphasizes that with this method of laparoscopy, a liver biopsy can be taken with less danger than usual. The most important part of the publication is the illustrations, which are partly photographs and partly drawings by Max Landsberg. Anyone who has done his first laparoscopy will remember the astonishment he felt at seeing the different colors of the abdominal organs and the difficulty in evaluating the findings. Kalk's illustrations facilitate all studies in this field. Rare conditions, such as carcinoma of the gallbladder, are shown.

The second part of the book consists of a short introduction to gastroscopy by W. Bruehl. Here, too, the illustrations are most helpful. The book is well printed, published in German, with a fair summary of the literature in this field. It can be recommended to internists and gastroenterologists.

Franz J. Lust

FOOD AND YOU. Edmund Sigurd Nasset, Ph. D., 100 pages. Charles C. Thomas, Springfield, Illinois, 1951, $3.00.

The author, Professor of Physiology at the University of

Rochester, Rochester, New York, being well versed in the subject of nutrition, wrote the present book as a guide for his two daughters, Laura and Susan, one studying architecture and the other chemistry. (It would be only fair if one of the daughters, in appreciation of what is more than a fine gesture, would write a book on architecture for the Professor, in case he is intending to build a new home.) The book goes into the composition of food, the requirements of man, the digestion and absorption of food, the utilization of protein, fat, carbohydrates, vitamins and minerals. A final chapter on "common sense about food" will especially appeal to most liberal readers. He stresses the irrational nature of food aversions. He lists 7 groups of foodstuffs and states that the average person's nutritional needs will be satisfied if he eats at least one serving every day from each of these 7 basic food groups. One must agree that this is a likable and accurate little book which many people would enjoy.

THE ODYSSEY OF MODERN DRUG RESEARCH. Robert Burlingham. Published by the Upjohn Company, Kalamazoo, Mich.

This attractive volume deals with pharmaceutical manufacture, its science and economics. The illustrations, particularly the colored ones, are beautiful. Although the book is definitely an Upjohn inspiration, it is, nevertheless, extremely interesting, and acquaints the reader with a few of the tremendous difficulties which American houses have overcome and are constantly meeting, for the good of all.

TECHNICAL METHODS FOR THE TECHNICIAN. Anson Lee Brown, B. A., M. D., Anson L. Brown, Inc., 41 S. Grant Ave., Columbus, Ohio, 1951, $10.00.

This 800 page book is extremely informative and therefore useful. It covers the whole field of practical clinical laboratory work and will prove quite indispensable to the practicing laboratory technician. We highly recommend it.

GENERAL ABSTRACTS OF CURRENT LITERATURE

KALK H.: *Diseases of the stomach, such as gastric and duodenal ulcers caused by military duty.* Medical Department of Stadtkrankenhaus Kassel-Wilhelmshoehe (Die Medizinische Welt 1951, Nos. 16 a. 17)

In the genesis of peptic ulcers constitutional and environmental factors are discussed. The last war has decisively shown the influence of exogenic factors. A large increase of peptic ulcers has been noted in civilians. During the late war temporary gastric (peptic) ulcers increased in the Berlin area, more than two times the normal pre-war average. Especially gastric ulcer temporarily increased three to six times more than the duodenal ulcer.

The reason for this greater incidence of peptic ulcers in civilians can be accounted for by the increased work load, irregular meals, diminution of food proteins and psychological troubles such as nightly bombings.

The increase was also frequently noted in the men of the armed forces, but surprisingly enough, it was more frequent in the home front troops and military hospitals, than in the troops on the far flung fronts. The first signs of peptic ulcer in 70% of cases in military hospitals had their start in the pre-war period. An examination of ulcer cases in these hospitals has shown that nearly 85-90% of these cases in the Army (Wehrmacht) showed no effect or background of military duty in the genesis of these ulcers. On the other hand it seems that military service provides a possibility of relapses.

In contrast to the ulcers the onset of gastritis is favored in war and front line service.

Our own evaluation of brain wounded soldiers in hospital has shown no increase of peptic ulcers in these cases and is in accordance with the findings of BODECHTEL and SACK. It seems that chronic ulcers are extremely rare following brain and head lesions.

In spite of the obviously small possibility of acute peptic ulcers becoming chronic one should appreciate that initial ulcer disease may be a product of stress from military service. But when clinic or hospital treatment is successful in healing peptic ulcers without disturbance of stomach function there is no basis for line of duty for later relapses. However, if signs of the first ulcer are remaining from military service, such as scarring, alterations like stenosis of pylorus, scar shortening of the lesser curvature, sandglass stomach and deformity of the bulb, then the ulcer disease must be regarded as due to line of duty in such cases. The possibility of a reduction of employability must be noted on an average of 30-40% for most of the cases with peptic ulcers.

When a soldier has had ulcers before his military service and a fresh ulcer is started during his service it must be considered as in line of duty but only for this particular ulcer. If hospital treatment is successful in healing a recurring ulcer and another ulcer arises later after military service it is not to be considered as in line of duty—with this exception—that, when the ulcer seen in military service has brought about a change for the worse, which is determining for the further course of ulcer disease, which means it is followed by gross alterations which arise in the course of ulceration such as stenosis of the pylorus, shortening of the lesser curvature, hourglass stomach and extreme deformities of the bulb.

When an ulcer perforates during military service, it must always be regarded as a change for the worse and which is determining factor for the future course of ulcer disease; that is why patients with perforated ulcers which are operated on have the tendency for recurring ulcer and post-operative disturbances.

Post-traumatic ulcers caused by blows, shocks and falls are so rare, that their appreciation in line of duty is to be correctly controlled in each case for special factors.

The similar statement is necessary for the appreciation for ulcers following injuries of the head and brain. Ulceration caused by heat and cold are known but the significance is provisional on their time connection with this event.

Under the specific influence of military duty gastritis occurred often. The assumption of a gastritis is entitled to be considered in line of duty but only for acute cases of gastritis which slightly heal under relevant treatment. The appreciation of chronic forms of gastritis in line of duty can only be considered when caused through the influence of long damage in front line duty which prohibits early treatment so that a chronic form of the disease is made possible with disturbances of acid production and gastric glandular deficiency (anadenie, achylia). This is also possible by long lasting pathological alteration of proteins caused by heavy injuries with concomitant infection of long duration, by chronic infectious diseases during army service.

Also in this war—but not so frequent as in World War I—dysenteria has produced conditions like chronic gastritis with sub- or anacidity, enteritis with disturbances of function of other intestinal glands (pancreas, small bowel). By these forms of chronic gastritis with achylia distinct sequelae diseases will arise—likewise after World War I—such as pernicious anemia, achylic chlor—lack—anemia sprue and pellagra diarrheas, cancer of the stomach, fatty degeneration of the liver incipient to cirrhosis. Also these diseases ought to be appreciated as diseases incurred in line of duty.

ROCHA, O. DE L., RODRIGUES, D. AND CHARVAGLIA, D.: *Os efeitos do cloreto de tetra-etil-amonio sobre a secrecae gastrica na fase interdigestiva (The effects of tetra-ethyl-ammonium chloride on gastric secretion in the interdigestive phase).* Rev. Brasileira de Gastroent., 2, 5, 1950, 501-506.

Experimental observations were made on 12 patients in an attempt to evaluate the effects of TAC on the interdigestive phase of gastric secretion. One patient had a gastric ulcer and 6 had duodenal ulcers, all proved by x-ray films. The remaining 5 cases were diagnosed as follows—dysentery, hypochromic anemia, chronic arthritis, chronic cholecystitis and gastroduodenitis. TAC decreased gastric secretion, and what was of greater interest, it reduced both the free and total acidity in these cases.

HAYNES, L. L. AND CRONEMILLER, P. D.: *Complications of Meckel's diverticulum.* U. S. Armed Forces M. J., 1, 11, Nov. 1950, 1329-1355.

The nine cases of Meckel's diverticulum reported illustrate the following complications,—hemorrhage and ulceration, inflammation, obstruction and intussusception. In all laparotomies, search for a Meckel's diverticulum should be made when the pathological changes found in the appendix are insufficient to account for the symptoms and signs present.

CRAIG, C. F.: *Amebiasis and the complement-fixation test.* U. S. Armed Forces M. J., 1, 11, Nov. 1950, 1337-1342.

A positive complement-fixation test disappears within 2 to 4 weeks following elimination of *E. histolytica.* Its persistence after this period, indicates that a focus of infection is still present in the body, perhaps in the liver, so that hepatic abscess later may form. In many acute cases of amebic dysentery the body is unable to produce a positive test, while strong positives may occur in cases practically symptomless but with silent ulceration. At present the complement fixation test is merely a diagnostic aid, and should not be attempted until careful stool examination, cultures and sigmoidoscopies have been completed. False positives and false negatives may be obtained. The antigens now used are not made from pure cultures of *E. histolytica* and are always contaminated by bacteria. False positives were obtained in some cases of chronic ulcerative colitis but few such reactions have been reported in other diseases. Too much refinement of the antigens has impaired the value of the test as a diagnostic procedure in amebiasis. When a positive test is obtained, it is strong presumptive evidence that infection with *E. histolytica* is present and treatment should be administered. The test is of great value, however, as corroborative evidence in discovering carriers, in diagnosing hepatic abscess, in controlling treatment and in testing out proposed amebicidal drugs in animals.

RAFFENSPERGER, E. C.: *Elevated serum pancreatic enzyme values without primary intrinsic pancreatic disease.* Ann. Int. Med., 35, 2, August 1951, 342-51.

The author has found elevation of serum pancreatic enzymes in some cases of the following diseases,—perforation of peptic ulcer, small bowel obstruction, acute peritonitis, diaphragmatic hernia with torsion and strangulation of the stomach and in 3 cases associated with renal impairment. In none of the cases was primary intrinsic pancreatic disease present and in none was the serum amylase higher than 400 mg. percent. The majority of the serum lipase values were between 1.5 c.c. and 4.0 c.c. Perhaps soiling had produced a peripancreatic peritonitis with partial blocking of the outflow of the external pancreatic section,—but this is pure speculation. It might seem that abdominal pain associated with a serum amylase value of less than 500 mg. percent suggests a diagnosis of perforated peptic ulcer, while an elevation above 500 mg. suggests acute pancreatitis.

SILVIS, R. S., CAPT. M. C., U. S. N.: *Liver suture.* U. S. Armed Forces. M. J., 11, 8, Aug. 1951, 1205-11.

Silvis describes the use of ribbon catgut on a long needle for surgical repair of the liver. Ribbon catgut was developed years ago by urologists for suture of the kidney. The only available needle of sufficient length with an eye large enough to permit the threading of ribbon catgut is the autopsy needle.

MALOUF, S. D.: *Intussusception in the adult.* J. Indiana State Med. Assoc., 44, 9, Sept. 1951, 841-5.

The author presents a case of intussusception in an adult woman due to a dysontogenetic type of new growth which was cured by a one-stage primary resection with anastomosis. Intussusception in the adult is a chronic and relatively uncommon disease. The diagnosis is difficult and treatment is entirely surgical. The dangers of procrastination are as dangerous as in children.

RADKE, R. A., COL., M. C., U. S. A.: *Amebiasis; evaluation of new therapies.* U. S. Armed Forces M. J., 11, 8, August 1951, 1231-34.

For five years the author has been studying the effects of quinacrine in the treatment of amebiasis. He found that some additional agent was needed to combine with quinacrine to destroy the organism in its cystic stage and for this purpose carbarsone was the most promising. His best results were obtained with this combination but almost equally good results were obtained when aureomycin was added to the other two. Either of these combinations gave far better results than a combination of chloroquine and carbarsone or the use of aureomycin alone. Most patients can be treated as out-patients, using either of the two preferred combinations. Toxic reactions from carbarsone must be carefully watched for.

LANE, J. D.: *Large solitary gall stone.* Miss. Valley Med. J., 73, 5, Sept. 1951, 245.

Lane removed a gall stone from a man of 73, 7 c.m. in length (2½ inches) and weighing 39.5 grams. (The largest stone on record is Ritter's which weighed 110 grams). The patient had complained of abdominal pain and belching for 20 years. Appendectomy had failed to relieve him. Later, mild jaundice and itching of the skin occurred. Although he refused to take the contrast medium, a satisfactory x-ray picture of the stone was obtained by the following x-ray technique—Position PA; Bucky, large focus tube, K. V. 70 MA 80; distance 30 inches, exposure 1.9 seconds.

BANKOFF, M. L.: *Use of rectal suppositories in the treatment of migraine headache.* J. Indiana State Med. Assoc., 44, 9, Sept. 1951, 836-8.

Bankoff describes the use of a new rectal suppository (E. C. 112, Sandos), containing 2 mg. ergotamine tartrate and 100 mg. caffeine in the treatment of vascular headache. Seventy-nine percent of a group of 48 patients who had previously responded well to hypodermic Gynergen or DHE 45 reported good to excellent results with the use of rectal inserts at the onset of each attack over a trial period of 8 months.

BARSH, A. G.: *Primary malignant epithelial tumors of the small bowel.* Radiology, 57, 2, Aug. 1951, 177-185.

Primary cancer of the small intestine is rare, accounting for only 3 percent of malignant lesions of the gastrointestinal tract. The types of primary epithelial malignant lesions in the small bowel are,—carcinoma, carcinoid, and melanoma. Blood in the stool is fairly constant in carcinoma but not in carcinoid. A careful x-ray examination is the most accurate means of diagnosis. The author reports 6 cases of primary epithelial malignant tumors of the small intestine.

YAMASAKI, K. AND CAMPBELL, K. N.: *The repeated development of acute abdominal symptoms from an undiagnosed foreign object in the large bowel.* Alex. Blain Hosp. Bull., 10, 3, Aug. 1951, 74-77.

A report of a case of a boy of 15 with abdominal symptoms in whom a 7 inch lead pencil was surgically removed from the descending colon. Previously the symptoms had led to a useless appendectomy. The authors dilate upon the various objects found in the bowel and their means of introduction.

BRUECKEL, KURT W.: *Intestinal Function and Nervous System.* Medizinische Welt, 20, 516-519, 1951.

In the eyes of the author it is not yet possible to overlook and limit sufficiently the biological significance of the hormone-like active substance Gastrine, Enterogastrine, Enterocrinine, Villicrinine etc., more detailed characterized in recent times. It seems sure, that after anesthesia of the mucous membrane, that means, after elimination of submucous nervous plexus, chemical stimulations from the cavity of the intestine will be answered no more. The movements of peristaltic and segmentation nevertheless remain undisturbed, even after the mucous membrane and Meissner's plexus have been removed. As a rhythmic intestinal function is held up also after complete separation from the CNS or the sympathetic nervous system, we must assume a comprehensive autonomy of the plexus in the intestinal walls. The vegetative connective pathways may therefore be less apt to produce than to influence already existing movements in a furthering or inhibiting way. Predominantly, the intestinal volume is regarded as the adequate stimulation for movement.

AMER. JOUR. DIG. DIS.

The effect of the complete isolation from abdominal vagal influences has been studied intensely also in humans since the practice of vagotonia. Atony of the stomach usually stands in the foreground. After the investigations of Dale and Feldberg, choline or acetyl-choline is supposed to be the stimulating substance for intestinal motility. Recently a convincing proof on the humoral transferability of the nervous impulse could be elaborated by Vogt. He made the interesting observation that the agent, freed by vagal stimulation, seems neither choline nor histamine-like, but represents an atropine-insensitive intestinal active substance. Accumulations of "Darmstoff" are to be found in the outer parts of the intestinal walls, contrarily to acetylcholine. According to paper-chromatographic studies, v. Euler and Gaddums substance "P" contains "Darmstoff" too. Presumably, Vogts "Darmstoff" does not yet represent its pure active form.

Stimulation of Splanchnicus Nerves usually leads to an inhibition of small intestinal motility. Sometimes, constipation can be done with by operative elimination of the Sympathicus. After combined sympathectomy and vagotomy an acceleration and striking monotony of motility mechanism results. Hypermotility, hypersecretion and hyperemia are prompt consequences of coeliacus extirpation. Inhibitory reflexes running over the area of the retoperitoneal plexus and the spinal cord may be eliminated by coeliacus or spinal anesthesia; in peritonitic reflex paralysis similar practices display uneffective. Here surely the reflexes inhibitions run mainly over intramural or wall-near pathways.

Signs of missing retroperitoneal plexus in the upper abdomen, have been observed by the author in an abdominal form of Hodgkins Disease. A complexity of symptoms called "Coeliacus-Ausfalls-Syndrome" is amply discussed in a male patient of 38 years, suffering from an inoperable pancreas head cancer. Diagnosis was clued intra vitam because of uncurable, partly bloody-mucous stools and a characteristically impaired intestinal motility (x-ray study). Autopsy revealed a plate-like cancer infiltration of the plexus coeliacus with necrobiotic changes in the ganglionic cells. According to the author's opinion, therapy-resistant persisting diarrheas are mainly in tumors of the pancreas (Friedenwald and Cullen, Berk) due to similar alterations. Also in the abdominal forms of porphyria and chronic saturnism such connections must be assumed. Corresponding experimental proofs already have been delivered by Gruenberg.

The characteristic secretory insufficiency, the tendency to hyperchrome anemia and perhaps also the behaviour of duodenal secretion in sprue, described by Smart and Daley, exceed after the author's opinion, the extent of what is to be expected after elimination of the plexus coeliacus. Relations between a disturbance of the retroperitoneal upper abdomen plexus and the sprue or coeliacic symptoms, as Freise and Wallenta try to construe, are to be refused, at least primarily in pathogenetic aspects. In this connection the transit from "chronic" small intestine insufficiency to the typical symptomatology of sprue is described on clinical observations. Finally, neuron forms of tumor in the intestinal tract and pathologic changes in the Biermer-Addison-Anemia are discussed and a possible significance of the neurogen accompanying cells in Meissner's plexus (Feyerter) is pointed out.

K. W. Bruckel

SHORTHOUSE, P. H. AND KING, R. C.: *Idiopathic hypochromic anemia in young adult males.* Brit. Med. J., Aug. 4, 1951, 256-59.

20 cases of idiopathic hypochromic anemia are described in young men. Nail changes were present in some, and most of them showed a definite tendency to immaturity. Achlorhydria or hypochlorhydria was present in 16 of the remainder, normal gastric acidity was present in one and hyperchlorhydria in three. Blood pictures rapidly improved and in most cases became normal on treatment with adequate amounts of iron. The anemias probably were due to an increased demand for iron coupled with defective intestinal absorption. The authors do not, however, prove that faulty adsorption of iron played a part.

COCKBURN, W. C., HARRINGTON, J. A., ZEITLIN, R. A., MORRIS, D. AND CAMPS, F. E.: *Homologous serum hepatitis and measles prophylaxis.* Brit. Med. J., July 7, 1951, 6-12.

Of 10 recipients of the same batch of plasma for measles prophylaxis, seven developed a severe form of jaundice and three of the seven died. Part of the same batch of plasma was fractionated and gamma globulin was prepared from it. Among 56 recipients of this gamma fraction, only one developed jaundice,—a boy of 12 who had received 8 ml. The risk of homologous serum hepatitis following the use of gamma globulin prepared from an icterogenic pool of plasma appears to be much less than that following the use of the unfractionated plasma, but it cannot be ignored. Children under 5 who have been held to be relatively unsusceptible to homologous serum hepatitis, may in some circumstances develop the disease, which may prove fatal.

MICHELS, A. G. AND HOERR, S. O.: *Spontaneous internal biliary fistula; a case of cholecystocolic fistula.* Cleveland Clin. Quart., 18, 3, July 1951, 184-189.

A case of cholecystocolic fistula is described. An accurate pre-operative diagnosis was made by means of a barium study of the colon and confirmed at operation. This complication of gall bladder disease can be avoided by early removal of the gall bladder.

HAMMER, J. M. AND HILL, E. J.: *Experimental ulcer produced by reversing the duodenum.* Harper Hosp. Bull., 9, 4, July-Aug. 1951, 129-131.

The authors describe a method of producing experimental ulcers in dogs by completely reversing the duodenum, then performing a gastrojejunostomy, using an oblique end-to-side anastomosis. An oblique anastomosis is made between the proximal duodenum and the distal jejunal segments. The starvation factor present in Mann-Williamson dogs is eliminated. Drug antagonisms developing in chemically produced ulcers are avoided. The percentage of animals developing ulcers is high enough so that the method can be used in ulcer problem studies. Special diets to maintain the animals are not required. The authors do not offer any explanation as to *why* this procedure should produce ulcers in dogs.

MEYER, M. M., LIEUT. J. G., M. C., U. S. N. R. AND JARMAN, J. A., COL. U. S. A. F. (M. C.): *Banthine in the treatment of duodenal ulcer.* U. S. Armed Forces M. J., 11, 8, Aug. 1951, 1165-68.

Banthine was found to lower gastric secretions both in acidity and in volume, and was regarded as an effective gastrointestinal antispasmodic and a useful adjunct to the medical management of duodenal ulcer. 21 patients (84 percent of the group) were returned to duty for periods of from 1 to 6 months on a maintenance dose of banthine and no other medication. It now appears that a greater number of patients with duodenal ulcer are able to lead a more nearly normal service existence with banthine than any previously used medication.

ZOLLINGER, R. M. AND ELLISON, E. H.: *Indications for surgery in gallbladder disease.* Illinois Med. J., 100, 2, Aug. 1951, 121-128.

Provided the patient's trouble actually is disease of the gallbladder or bile ducts, operation will give good results, provided it is thorough. Symptoms usually are relieved in those patients having stones in the gallbladder. Failure of the gallbladder to concentrate the gallbladder dye is not sufficient evidence that the gallbladder requires surgery. Whether or not to remove the gallbladder containing "silent" stones is always an individual problem. Acute cholecystitis requires prompt hospitalization. The common duct should be opened to search for stones in more cases. Typical colic after operation is often due to common duct stone or retained cystic duct stump.

TRACEY, N. L.: *Diagnosis of colonic lesions.* Am. Pract. & Dig. Treat., 2, 8, August 1951, 673-8.

For proctoscopy the author favors the left lateral Sims' position with the right leg drawn up to the chin. The guaiac test on the gloved finder is routine. The roentgenogram is the most helpful single aid in the diagnosis of colonic disease. Scout films and barium enemas are employed and found reliable except in lesions in the lower rectum and rectosigmoid. Repeated barium enemas sometimes are required for clarification of doubtful areas. Double contrast studies sometimes are indispensable, especially in carcinoma, diverticulitis, amebic dysentery and in colonic tuberculosis of the right colon.

DIABETES

New York — Inauguration of DIABETES, The Journal of the American Diabetes Association, was announced today by J. Richard Connelly, Executive Director of the Association. The new Journal, which will appear bimonthly beginning with the January-February 1952 issue, will be devoted to clinical and research reports on diabetes and related aspects of medicine. It will be the Association's official scientific and original publication, replacing its annual PROCEEDINGS and its quarterly DIABETES ABSTRACTS, both of which have been published for the past ten years.

DIABETES will be edited by Frank N. Allan, M. D., of the Lahey Clinic, Boston, Mass., First Vice President of the American Diabetes Association. Doctor Allan will be advised and assisted by a distinguished Editorial Board under the chairmanship of Charles H. Best, M. D., of the University of Toronto, Toronto, Ont., co-discoverer, with the late Sir Frederick Banting, of insulin and its use in the control of diabetes.

According to Doctor Best, "The major purpose of DIABETES will be to give the medical profession and particularly the practicing physician, information which will help him to improve the treatment of diabetes and allied disorders. The Journal will also be of interest to research scientists, since it will publish many of the important findings from the laboratories bearing on the problems of the disease. The scope of the Journal will be wide enough to include data dealing with all aspects of modern medicine that could have value for the physician interested in the therapy of diabetes or research in this field."

The Editorial Board of DIABETES includes the following outstanding physicians:

Edward L. Bortz, M. D., Associate Professor of Medicine, University of Pennsylvania School of Medicine, and past President of the American Medical Association;

Arthur R. Colwell, M. D., Professor and Chairman, Department of Medicine, Northwestern University Medical School, and President of the American Diabetes Association;

Jerome W. Conn, M. D., Professor of Internal Medicine, Director of the Division of Endocrinology and Metabolism and of the Metabolism Research Laboratory, University of Michigan Medical School;

Jonas S. Friedenwald, M. D., Associate Professor of Ophthalmology, Johns Hopkins University School of Medicine;

George M. Guest, M. D., Professor of Research Pediatrics, University of Cincinnati College of Medicine;

Blair Holcomb, M. D., Clinical Professor of Medicine; Director, George S. Cox Medical Research Institute, University of Pennsylvania School of Medicine;

E. Perry McCullagh, M. D., Head, Section of Endocrinology and Metabolism, Cleveland Clinic, Cleveland;

Leland S. McKittrick, M. D., Clinical Professor of Surgery, Harvard Medical School;

Alexander Marble, M. D., Clinical Associate in Medicine, Harvard Medical School and Consultant in Medicine, Veterans Administration;

Herbert H. Marks, Manager, Insurance Medical Statistics, Metropolitan Life Insurance Company, New York;

Franklin B. Peck, M. D., Assistant Professor of Medicine, Indiana University School of Medicine and Consultant in Medicine; Indianapolis General Hospital;

Henry T. Ricketts, M. D., Professor of Medicine, University of Chicago, The School of Medicine;

Randall G. Sprague, M. D., Consultant Physician, Division of Medicine, Mayo Clinic, Associate Professor of Medicine, Mayo Foundation, Graduate School, University of Minnesota, and Vice President of the American Diabetes Association;

Russell M. Wilder, M. D., Ph. D., Director, National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, U. S. Public Health Service;

Wallace M. Yater, M. D., Director, Yater Clinic, formerly Professor of Medicine, Georgetown University Medical School.

The following physicians will serve as Consulting Foreign Editors for DIABETES:

George R. Constam, M. D., Zurich, Switzerland;

Hans C. Hagedorn, M. D., Gentofte, Denmark;

Bernardo A. Houssay, M. D., Buenos Aires, Argentina;

R. D. Lawrence, M. D., London, England.

Assisting Doctor Allan in the work of editing the Journal will be Rosemary Murphy, M. D., Boston, Mass., Assistant Editor; William R. Kirtley, M. D., Indianapolis, Ind., Abstracts Editor; Groff Conklin, New York City, Managing Editor; W. I. Van der Poel, New York City, Art Editor.

In addition to original contributions and scientific reviews, DIABETES will also include abstracts of papers dealing with diabetes that appear in scientific and medical periodicals here and abroad. This abstract section will help make the Journal an indispensable reference tool for both clinical and research physicians, since it will bring under one cover the latest information about the disease.

A variety of material of organizational and historical interest will also be included in the Journal, such as news of the Clinical Societies of the Affiliate Diabetes Associations throughout the country, of which there are now nearly thirty. A book review department will be a feature, as will the usual sections for correspondence, Committee reports, and editorials.

A positive effort is being made to break with the traditional format of medical and scientific periodicals. Its typography, layout, and printing are all being planned so that it will lead the field in appearance, legibility and simplicity. The over-all dimensions will be 8½ x 11 inches and it will contain 96-112 pages plus cover.

The subscription rate for the Journal will be $9.00 a year for non-members of the Association; members will receive it without charge. Correspondence concerning both editorial and business matters and manuscripts of interest to the Editors, should be addressed to the Editorial Offices, DIABETES, American Diabetes Association, Inc., 11 West 42nd Street, New York 18, N. Y.

To The Editor:—

A number of technical journals have evinced an interest in bringing the library research services of Research Information Service to the attention of their readers. We feel that this unique library service might be of the same interest to the reading public of THE AMERICAN JOURNAL OF DIGES-

TIVE DISEASES. We are, accordingly, sending you a copy of the newly revised edition of the brochure, "For Economy in Research," which describes the research assistance available through our staff of subject specialists.

We invite your inspection of this booklet with the thought in mind that an article in your publication would be a timely and helpful solution to the general current problem of dwindling technical personnel. Dr. Robert E. Wilson, chairman of the Board, Standard Oil Company (Indiana), speaking at the Institute of Petroleum in London, pointed out the weakened state faced by industrial research. The availability of technical personnel is at a low ebb due to the decreased numbers of trained men coming out of the schools, government competition for defense research, and drafting of technical men for non-technical service. More than ever, in the face of rising costs and lessened manpower, the time-saving, money-saving initial step of any research project—namely, library research—should not be overlooked. . . All too often it is set aside with the consequent result of costly duplication of work. Often the reason for failure to follow the principle of "first things first" is lack of man-power or lack of library facilities.

RIS has both trained man-power and the library facilities. The John Crerar Library is the world's outstanding library devoted to science, technology and medicine. The combination of Research Information Service and the strong science collections of Crerar Library can make a real contribution to the research programs of the men who read your journal. We hope you will agree with us that a presentation of the service outlined in the brochure will be of interest to those who look to you for pertinent and up-to-date information.

Sincerely yours,
Herman H. Henkle
Librarian

Note: The Brochure of the Crerar Library may be obtained by writing to 86 E. Randolph St., Chicago, Ill.

NEW PRODUCT DORMISON

Manufacturer: Schering Corporation, Bloomfield, New Jersey.

Active Constituent: Methylparafynol (3-methyl-pentyne-ol-3), a pure, highly volatile liquid.

Action: Hypnotic, inducing calm, peaceful sleep.

Advantages: Free from habit-forming properties of barbiturates: rapidly metabolized; no cumulative action; no toxic effects on prolonged use. Has no prolonged suppressive effect; patient awakens refreshed, with no drug hangover or other after-effects.

Indication: Simple insomnia, where severe pain or agitated psychotic states do not co-exist.

Dosage: One to two capsules (250-500 mg.) should be taken just before patient is ready for sleep.

Packaging: Soft gelatin capsules, 250 mg. each; bottles of 100.

ANNOUNCEMENT
TWELFTH ANNUAL MEETING
of the
AMERICAN DIABETES ASSOCIATION

June 7-8, 1952

The Drake
Chicago, Illinois

SCIENTIFIC SESSIONS
Saturday afternoon, June 7
Sunday morning and afternoon, June 8

ANNUAL BANQUET
Saturday evening, June 7

Wives and friends of members are cordially invited to attend. Make your plans now. A reservation form for the banquet will be sent to you a few months prior to the Meeting.

HOTEL RESERVATIONS

This year we have been fortunate not only to secure *The Drake* as headquarters, but also to have a number of guest rooms assigned to us for use by our members.

We believe that there will be a sufficient number of rooms to accommodate our members during our own meeting, June 7 and 8, based on the results of the survey we made last summer on probable attendance at the meeting. *The number of rooms available during the American Medical Association's Annual Session, June 9-13, however, is limited.* Rooms will be assigned for those days on the basis of "first come, first served."

If the requests for reservations through the American Medical Association meeting exceed the number of rooms which have been assigned to us, arrangements have been made by The Drake with the Hotel Knickerbocker (located directly across the street from The Drake) for such accommodations.

The following procedure is suggested:

1. If you are going to attend only our meeting, send in the reservation card to The Drake.

2. If you plan to remain for the A. M. A. Session, either:

(a) Send in the reservation card to The Drake. Should your reservation be over and above the quota of rooms allocated to us, The Drake will make arrangements to transfer you to the Knickerbocker on June 9;

or

(b) If you wish, you may make arrangements with the Knickerbocker to stay there during our Meeting and the A. M. A. Session, which might preclude the necessity of changing hotels.

Correspondence in this case should be addressed to Miss Helen Clare, Hotel Knickerbocker, Walton Place, Chicago.

Summary: There should be a sufficient number of rooms at The Drake for members during our own Annual Meeting, June 7-8, and for most of our members through the American Medical Association Session.

We urge your prompt attention in making reservations.

NEW COMPOUND FOR BILE ACID THERAPY

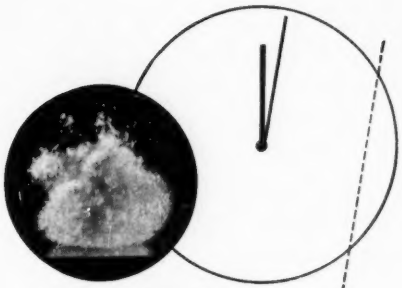
New York, N. Y.—Doxychol-AS tablets, a biliary stimulant with spasmolytic and sedative properties, have been introduced by George A. Breon & Company.

The new compound will be marketed as a companion item to Doxychol-K tablets, which contain strong hydrocholeretic and fat emulsification properties. When biliary insufficiency is accompanied by biliary spasm, Doxychol-AS tablets offer the added advantage of sedative and antispasmodic action.

A distinctly different label distinguishes the two products and in addition, Doxychol-AS tablets are green in color and scored, while the "K" preparation remains a white, unscored tablet.

Dosage for hepatic stimulation and spasmolysis is one or two Doxychol-

two-fisted
Enfozyme
Robins



a 30 second experiment

Drop a Syntrogel tablet in water. In less than 30 seconds you will note that it "fluffs up" to many times its size. This speedy disintegration increases the adsorptive surface approximately 10,000 times. Syntrogel goes to work in the stomach with equal speed. It adsorbs and neutralizes stomach acid, alleviates heartburn and provides prompt, yet long-lasting relief in most cases. Syntrogel gives symptomatic relief in peptic ulcer, dietary indiscretions and other conditions of gastric hyperacidity.

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Syntrogel®

Each Syntrogel tablet contains aluminum hydroxide, calcium carbonate, magnesium peroxide and Syntropan®.

'Roche'

"Doctor,

The best man to answer this question is, of course, your family physician. We suggest that you ask him the next time you pay him a visit.

I'd like to know...

what is a NUTRITIONAL TIME BOMB?"

"Nutritional Time Bomb" is science's dramatic name for an equally dramatic discovery about diet...the discovery that injuries caused by mistakes in diet may not reveal themselves until years later.

Like actual time bombs, these injuries remain hidden and unrecognized, exploding into symptoms when it is too late to do anything about them. Thus, the dietary wrongs of childhood may be visited upon the adult.

Such scourges of later life as tooth decay, goiter, high blood pressure, heart disease, anemia and hardening of the arteries are not necessarily caused by present diet faults. They may be the delayed effects of earlier injury, where a dietary deficiency has existed too long.

A sound child body—the foundation of a sound adult body—must be built from the food that goes into it. The true effect of a mother's care during childhood has only begun to be understood. And, since eating habits are formed in childhood, the conscientious parent can do much to insure the child against later penalties of wrong eating.

The protective foods should be used generously in the daily diet. Important among these are bananas—long prescribed by doctors as one of the first solid foods for infants. Bananas have a well-rounded supply of vitamins and minerals, and are distinctly beneficent in their action upon the digestive tract. Because of the many appetizing ways in which bananas can be served, as well as because of their nutritional value, they are now being more widely used than ever.

FOR HEALTH, EAT AND ENJOY A PLENTIFUL VARIETY OF THE "RIGHT" FOODS

UNITED FRUIT COMPANY

In Ulcer and Ulcerative Colitis
acid factor + mucosal resistance factor

"Although in experimental ulcers both the acid factor and the mucosal resistance factor are concerned, we have examples in which the acid factor predominates and others in which a decrease in the defensive properties of the mucosa predominates."*

*Peptic Ulcer. A. C. Ivy, M. I. Grossman and W. H. Bachrach, Blakiston Publishing Co., Phila., 1950.

Comprehensive therapy—whole duodenal substance, VIODENUM—provides an effective natural antacid plus factors which stimulate the mechanisms of repair and defense.

"Viodenum . . . increased the total volume of gastric secretion . . ." yet "Viodenum decreased the free acid . . ."*

*S. Krasnow, F. Steigmann and L. L. Hardt, Comparison of Effectiveness of Various Antacids on Gastric Acidity. Am. J. Dig. Dis., 17:242 (1950).

peptic ulcer

Dr. P. J. Raimondi treated 59 proven cases of duodenal ulcer with Viodenum. He states, "A decrease in the annual rate of recurrence of symptoms was observed in patients with the highest frequency of exacerbations prior to treatment."*

*P. J. Raimondi, Treatment of Duodenal Ulcers with Desiccated, Defatted Duodenal Powder. Permanente Foundation Med. Bull., 8:4 (October), 1950.

Dr. Garnett Cheney treated 30 cases of ulcerative colitis. He states that Viodenum offers ". . . great promise in effecting a complete remission and possibly even a clinical cure . . . whole duodenal substance or Viodenum apparently promotes healing of the bowel by supplying some anti-ulcer factor . . ."*

*Medical Management of Gastrointestinal Disorders. Garnett Cheney. Yearbook Publishers, 1950.

ulcerative colitis

"Duodenal substance (Viodenum) was administered to 35 patients . . . the results obtained in 85% of the patients were very favorable . . . Viodenum may be considered a very valuable aid in the therapy of chronic ulcerative colitis."*

*M. H. Streicher, J. Lab. Clin. Med. 33, 1633 (1948).

Viodenum, *the comprehensive approach:*

1. **Provides an effective natural antacid.**
2. **Provides factors which stimulate the mechanisms of repair and defense.**
3. **Provides natural mucin to soothe and protect irritated mucosa.**
4. **Stimulates gastric secretion yet decreases the free acid.**

Whole duodenal substance desiccated and defatted at body temperature.
Available in powder or ten grain tablets.

Literature available upon request

Viodenum

VIOBIN CORPORATION
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AS tablets three times a day. After the condition has been brought under control and if prolonged biliary stimulation is necessary, it is advisable to continue with Doxychol-K, containing only the bile acids in like quantities.

SHOCK STATE IN SURGERY SEEN "ROBBED OF DANGER"

Havana, Cuba—The shock state in surgery has been "robbed of much of its danger," according to Dr. Maurice L. Tainter, director of the Sterling-Winthrop Research Institute.

Recent advances in the treatment of surgical shock, stemming from continuous world-wide research in blood pressure stimulants since 1895 and now holding promise of saving countless lives, were outlined yesterday (December 14) by Dr. Tainter of the Academy of Medical, Physical and Natural Sciences of Cuba.

Dr. Tainter described dramatic effects achieved by l-arterenol, a hormone of the adrenal medulla, already used in many cases of sudden, profound shock where the patients' blood pressures had dropped so low they were not measurable.

The report was presented by Dr. Tainter on the occasion of his installation as a foreign member of the Cuban Academy, the scientific group corresponding to this country's National Academy of Sciences.

"Intimate mechanisms by which l-arterenol and epinephrine produce enormous energy changes in the microcosmos of body cells are still almost as obscure as they were fifty years ago," Dr. Tainter said. "But real progress in understanding the physiological importance of the autonomic nervous system has taken place during the present century, providing new additions to therapy."

Epinephrine was isolated in pure form from medullary extracts in 1897, and was recognized by 1904 to be useful in controlling hemorrhage, relieving asthma and prolonging local anesthesia, Dr. Tainter said.

"The second chromaffin substance, l-arterenol, however, was so elusive that, undetected, it followed natural epinephrine like a shadow through all the processes of purification," he explained.

Citing the significance of l-arterenol today, Dr. Tainter told of clinical reports which disclosed its important differences from epinephrine. By contrast with epinephrine, l-arterenol does not increase cardiac output and the pulse rate but does increase peripheral resistance, the clinicians found. It is believed that l-arterenol is a sympathetic ergone for general physiologic functions while epinephrine is for special purposes.

Dr. Tainter described the highlights of research in the field of adrenal medulla function and its application to therapeutics. The importance of the adrenal gland was emphasized in 1895 when extracts from its medulla were found to cause a marked rise in arterial blood pressure when injected intravenously. The extracts were found to mimic the action of the sympathetic nervous system. By 1910, a rapid development and introduction of synthetic epinephrine substitutes was underway. Today, there are more than 200 sympathomimetic amines which have been prepared, Dr. Tainter said.

Arterenol, he continued, is at once one of the oldest and the newest of the sympathetic drugs. Synthesis of a racemic compound was described in 1904, but resolution into its optical isomers was successful only in 1948 after years of investigation by research scientists. Chemists at the Sterling-Winthrop Research Institute isolated l-arterenol from commercial epinephrine in pure form, where it constitutes 10 to 18 per cent of the total. This companion hormone is now produced synthetically and is marketed by Winthrop-Stearns Inc. under the name of Levophed.

Dr. Tainter described several dramatic cases reported in medical journals, where l-arterenol proved life-saving to shock patients. Its prompt action, easy controllability and ability to provide vasomotor tone without preventing the repair of normal vasomotor mechanisms following shock were said to have robbed the so-called irreversible surgical shock of much of its dangers.

PAULY NAMED TO HEAD PHARMACY DIVISION

Rensselaer, N. Y.—Dr. Rudolph J. Pauly has been appointed director of the pharmacy division of the Sterling-Winthrop Research Institute, it was announced by Dr. Maurice L. Tainter, director of the Institute. Formerly assistant director of the pharmacy division, Dr. Pauly replaces Edward D. Davy, who has retired.

Dr. Pauly was professor of pharmaceutical chemistry at the American University of Beirut, in the Lebanese Republic, from 1927 to 1949 and director of its School of Pharmacy and the University hospital pharmacy. He was decorated by the Lebanese government with the Chevalier de L'Ordre du Sedres.

Dr. Pauly received a B. S. and M. S. at Whitman College, Oregon, where he was later assistant professor, and a Ph. D. at the pharmacy school of the University of Wisconsin. He did graduate work in medical chemistry at Yale and taught chemistry there. He is a member of the American Pharmaceutical Association, the American Chemical Society, the American Association for the Advancement of Science, and other organizations.

LILLY TO FEATURE "MEDICINE IN AMERICA" PAINTING SERIES

As part of a widespread campaign to publicize the unique qualities and benefits of American medicine, Eli Lilly and Company is featuring a "Medicine in America" series of paintings in its bimonthly house organ, *Physician's Bulletin*, through the year 1952.

Six scenes have been chosen to illustrate representative aspects of America's unique patient-physician relationship. These will appear as a cover-flap in each issue and may be torn out and displayed in physicians' waiting rooms. The important message the paintings tell will thus have the attention of those who will have great influence on the form in which medicine in America will be practiced.

The pre-eminent place which American medicine holds in the world today, as the *Physician's Bulletin* series points out, is largely due to the many freedoms that patients as well as medical research and medical practice enjoy in this country. At this time of crucial decision, however, only an enlightened people, fully aware of the rich heritage of their freedoms, will act effectively to perpetuate those freedoms.

Eli Lilly and Company is giving

similar expression to these realizations by its membership in the Health Information Foundation. This organization, of which Admiral W. H. P. Blandy, U. S. N. (Ret.), is the president, is a fact-finding group now working in full gear via 221 radio programs, television, the press, special publications, and other lines of communication to stimulate the American people to face their own medical needs squarely and with their own community resources. The chief inspiration behind this work is primarily a deep faith in the will of the people and in the effectiveness of individual responsibility forcefully expressed at local levels.

The "Medicine in America" series of paintings, executed for Eli Lilly and Company by several well-known artists, will thus help to emphasize the conviction that an aroused home-town America is the most formidable bulwark against the many threats to freedom in our country.

SENIOR CHEMIST

Maltbie Laboratories, Inc., Newark, N. J., announces that Dr. Su Ming Wang, Madison, Wisconsin, has joined its research staff as senior chemist in pharmaceutical research and development and that Mario J. Cerro, Brooklyn, New York, is now bacteriologist in charge of ampul production.

Dr. Wang is a graduate of Weyland Academy in China and received his B. S. degree from London University. He is also a graduate of Washington State College with the degree of M. S. and of the University of Wisconsin with the degree of Ph. D. He has had industrial experience with Glaxo Laboratories, London, as a pharmaceutical chemist.

Mr. Cerro is a graduate of St. John's University with the degree of Bachelor of Science and did graduate work in bacteriology at St. John's. He has worked for Carlo Erba, Inc., as a bacteriologist and the U. S. Vitamin Corp. as research pharmaceutical chemist.

EFFECTIVENESS OF CITRUS FRUIT AS AN ANOREXIC AGENT

The use of citrus juice 30 to 60 minutes before meals as an appetite appeaser is reported to have been effective in gaining a high degree of adherence to a prescribed dietary regimen for weight reduction in a group study conducted by Norman Jolliffe and Elmer Alpert of the Bureau of Nutrition, New York City Department of Health.

Forty-two unselected subjects, averaging 41.3 pounds overweight, were under observation for at least four consecutive weeks. They were instructed to use four ounces of orange juice or grapefruit juices as an anorexic agent 30 to 60 minutes before their noon meal and again at a similar interval before the evening meal. Besides the citrus juice allowance, counted as 100 calories daily, each subject had prescribed for them a low calorie diet ranging between 1,000 and 1,400 calories.

The predicted total weight loss for the 42 subjects, assuming an undeviating adherence to the regimen, was 786.7 pounds. The observed weight loss was 603 pounds. From this a "performance index" of 76.6 is calculated. The average of individual indexes was 78.8. These results are regarded as indicating a high degree of adherence.

The study is reported in *The "Performance Index" as a Method of Estimating Effectiveness of Reducing Regimens, Postgraduate Medicine, 9:106-115, 1951.* As a measure of the degree of adherence to a prescribed diet by groups of people, the group performance index method is believed by the authors to have advantages over a simple comparison of the average crude weight loss per week. People of both sexes with varying ages, heights, degrees of overweight and of physical activity can be included in the same group. Effectiveness of management can be compared when diets of varying sub-calorie values are used. Similarly, quantitative comparisons of regimens employing various adjuvants become possible.

Predicted weight loss for each subject was estimated from the calorie deficit shown by deducting calorie intake from estimated calorie expenditure. The observed weight loss, expressed as a percentage of the predicted loss serves as an index of the effectiveness of management. Errors inherent in the individual performance index tend to balance each other in the group performance index if a sufficient number of subjects is studied, the authors state. Among the 42 subjects were 8 men and 34 women, varying in age from 17 to 62 years. The amount of overweight ranged from 11 to 131 pounds. The average weight loss per week was 1.90 pounds

"The use of about 50 calories of citrus fruit taken in the late morning and afternoon 30 to 60 minutes before the next meal has very definite advantages as an anorexic agent," Jolliffe and Alpert report. "Most people like it. It is readily available in homes either fresh, canned, or concentrated and frozen or refrigerated. Practically every restaurant, lunch counter and soda fountain has it. It supplies about 10 to 15 gm. of readily available carbohydrate to combat hypoglycemia which may occasionally occur about that time. Its use at that time tends to prevent the subject from consuming foods high in calories."

PONTOCAINE SPINAL ANESTHESIA PROLONGED BY FIFTY PER CENT

Prolongation of Pontocaine spinal anesthesia by approximately fifty per cent through the addition of the vasoconstrictors Neo-synephrine or epinephrine is reported by Drs. John J. Bonica, Philip H. Backup and W. Howard Pratt of the Tacoma General Hospital in *Anesthesiology* (12:431, 1951).

Pontocaine itself, they point out, gives comparatively long lasting spinal anesthesia which can be intensified by the vasoconstrictors. The paper is based on a controlled study, in which 631 nerve blocks were administered to 487 patients, both for therapeutic purposes and for a wide variety of surgical procedures.

A control group of 191 received the spinal anesthetic Pontocaine alone; and one of three vasoconstrictors—Neo-synephrine, epinephrine and ephedrine—was administered in addition to the anesthetic to each of three groups of approximately 135 patients.

The doctors found that Neo-synephrine increased the duration of objective analgesia to an average of 4 hours and 27 minutes, an increase of 50 per cent over the control group. Subjective sensory blocks lasted an average of 6 hours and 22 minutes with Neo-synephrine, 42.5 per cent higher than the control group. Similar results were obtained for the duration of motor paralysis.

Pontocaine itself may be used in

much smaller doses than was formerly advocated, according to the report. In small doses, it was found to afford spinal anesthesia of two hours or more without the addition of other preparations. It had previously been assumed that Pontocaine produced anesthesia lasting from one and a half to two hours, and that vasoconstrictors could prolong this action by as much as 100 per cent.

A medical department is like a right hand to a pharmaceutical firm but it ought to know what the other hand is doing, E. Claiborne Robins, president of the A. H. Robins Company, Inc., Richmond, Va., told the mid-year meeting of the American Pharmaceutical Manufacturers' Association in New York.

By the "other hand," Mr. Robins meant the sales department, he explained during a symposium on "The Place of the Medical Men in the Pharmaceutical Industry" on November 28.

"The medical department sits in at all our sales meetings and takes an important part in conducting sessions at the training schools for detail men," the speaker said.

In this way, he continued, representatives go into the field briefed with data that have the force of medical authority behind them—and no other. Exaggerated claims have no chance to gain currency.

"Because the pharmaceutical industry, like Caesar's wife, must be above suspicion, it is important that products be presented in an absolutely truthful and accurate manner that can be verified medically."

Mr. Robins added that it works both ways—a medical department builds the morale of the sales force by giving them a source to which they can turn for the answer to any questions that may be raised by doctors on whom they call.

THE STORY OF THE MERCK INDEX

Announcements of the forthcoming Sixth Edition of *The Merck Index* should be of interest to the large number of chemists, pharmacists, physicians, dentists, veterinarians, botanists, and members of allied professions who are familiar with previous editions of this widely used reference work, and from whom thousands of letters of inquiry have been received since supplies of the preceding edition were exhausted during World War II.

Historically, the first edition of this comprehensive reference work, then known as *Merck's Index*, was published in 1889. A much smaller book than later editions, the title page read in part: "Merck's Index of Fine Chemicals and Drugs for the Materia Medica and the Arts—Comprising a Summary of Whatever Chemical Products Are Today Adjudged as Being Useful in Either Medicine or Technology." There followed a lengthy foreword, describing the purpose and contents of the book, and concluding with the expressed wish that this edition "may be a Welcome Visitor not only to whomever it calls upon; but may prove so useful as to be asked to 'come again'."

The Second Edition, bearing the title *Merck's 1896 Index* and published early in that year, was designated as "An Encyclopedia for the Physician and the Pharmacist of the Chemicals and Drugs Used in Medicine, in Chemistry, and in the Arts."

In the Preface to this edition it was stated, in part, that: The purpose of *Merck's Index* is to provide, for all who have to do with Medicinal and Chemical matters, *one handy volume*, as a ready means of quickly and reliably answering questions of fact that may arise in *any* direction, in the midst of their work. Instead of having to consult *several* Materia Medica manuals, Chemical dictionaries, Dispensatories, or other works of different scopes, the reader will here find *all* those various directions of research simultaneously considered, in *one* alphabetic, concise, and lucid series of descriptive paragraphs, under the heads of the several substances concerned.

The Third Edition was titled *Merck's 1907 Index* and was described as "An Encyclopedia for the Chemist, Pharmacist and Physician." In the Preface to this edition, it was stated that: In order to bring the Index up to date in this edition we have added the newest products, adopted the latest nomenclature, consulted the most modern authorities, and, for the Merck products, verified the data in our laboratories and our works. Furthermore, we have added the crude drugs of commerce and have indicated under each drug the dose of its extracts, tinctures, fluid extracts, etc., instead of grouping all extracts, tinctures, etc., together as in the previous editions of the Index.

The Fourth Edition of *Merck's Index*, published in 1930, contained the following prefatory statement: *Merck's Index* perhaps needs no introduction; rather is an explanation due for the tardy publication of this the Fourth Edition—over two decades after the appearance of the previous issue. This delay was caused largely by the complete interruption of work on the book in both laboratory and editorial rooms during the World War.

In January 1940, the Fifth Edition of this well-established and highly regarded reference work appeared in a new form and dress, and with its title changed to *The Merck Index*. This edition was designated as "An Encyclopedia of Chemicals and Drugs for the Chemist, Pharmacist, Physician, Dentist, and Veterinarian." It comprised 1,060 pages—almost twice the number of the previous edition—and it contained more than 5,900 descriptions of individual substances.

Some of the outstanding features of the new Sixth Edition are: Approximately 20,000 names of chemicals and drugs, alphabetically arranged and completely cross-indexed so that the user can find any listing by looking under either the trade, chemical, or common name of the substance.

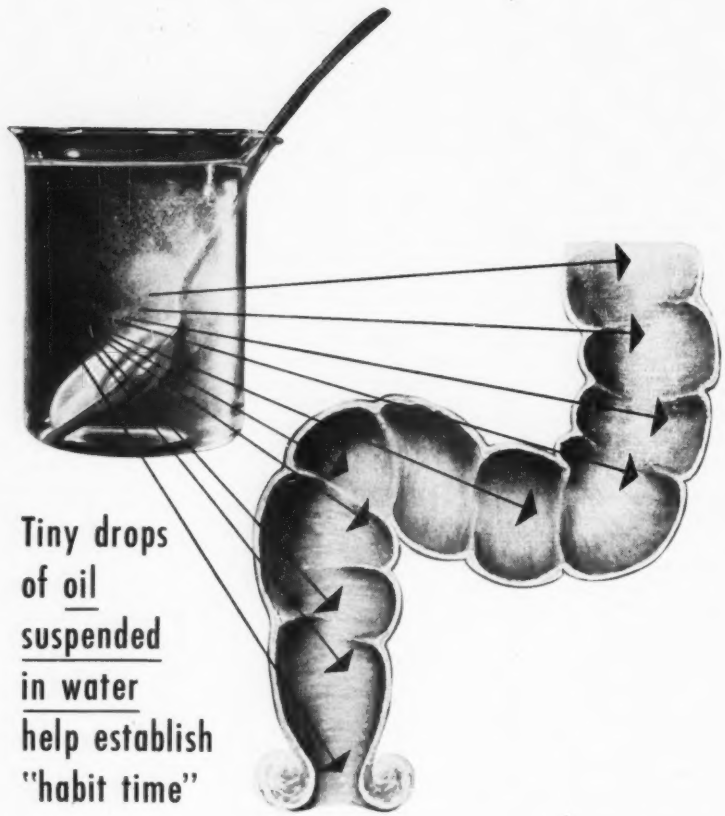
More than 2,000 clear, easy-to-read structural formulas.

Each main entry indicates the preferred chemical name or other chemical names, common or popular names, generic and trade names. Trade-mark listing is as complete as possible and thoroughly cross-indexed.

Properties and sources of substances, preceded by methods of preparation, with literature references, are given, followed by an indication of uses, whether industrial, medical, or veterinary.

Hazards, toxicities, and other safety factors are stressed.

Indication is given of commercial



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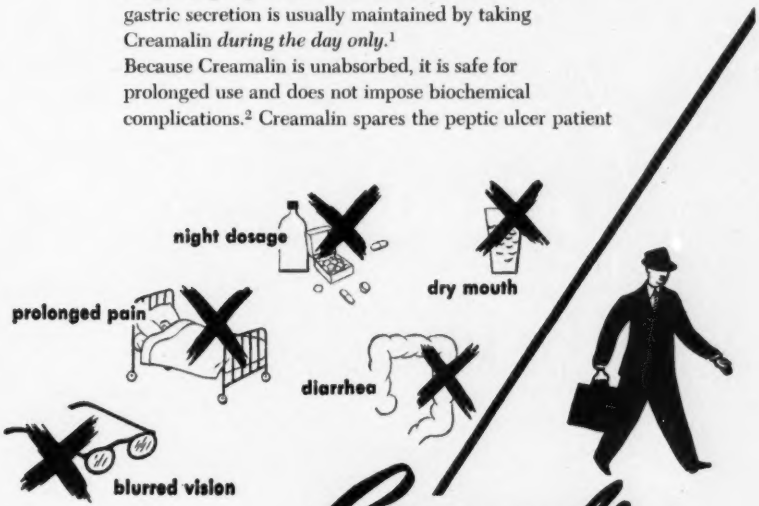

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2. Jordan, Sara M.: *Ann. West. Med. & Surg.,* 4:133, Mar., 1950

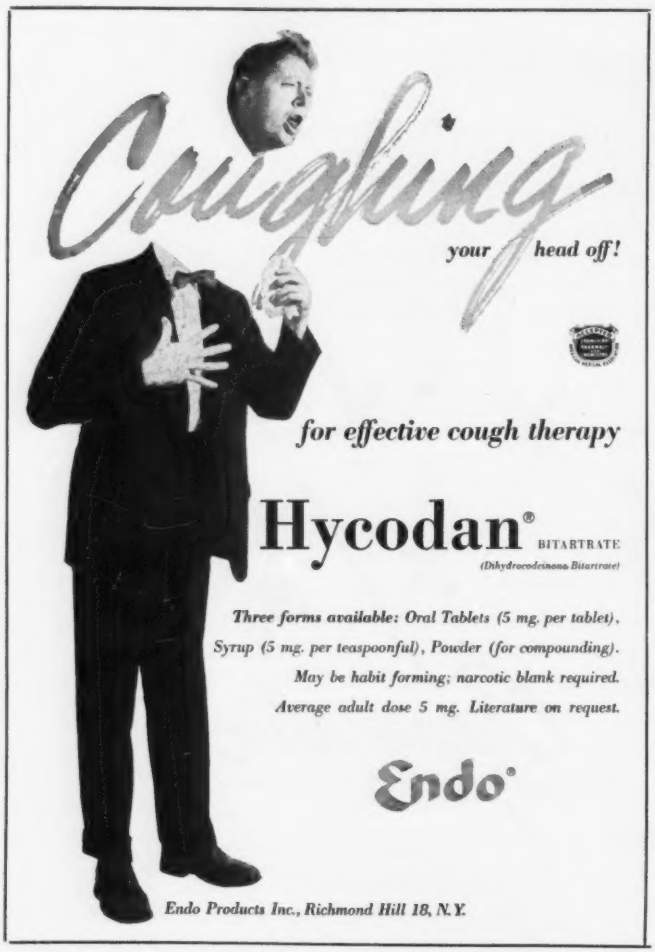
availability and grades, such as U.S.P., N.F., and reagent.

Empirical formula, molecular weight, and percentage composition are given for all chemicals having a *definite* structure.

Approximately one hundred pages of appendices contain the following valuable sections, revised and brought up to date: Coal-tar colors for foods, drugs, and cosmetics; indicators; tables of metric and United States systems of weights and measures and their equivalents; thermometric equivalents; specific gravity comparisons; antifreeze mixtures; cooling mixtures; constant humidity solutions; boiling temperatures of liquids; solidification temperatures of liquids; refractive index of liquids; specific gravity of liquids; specific gravity of solids; weights of liquids per gallon; saturated solutions; percentage solution tables for apothecaries and metric systems; first aid in poisoning; radioactive isotopes commonly used in medicine; radioactive isotopes of interest to the chemist; named organic reactions; atomic weights and their multiples and logs.

The Sixth Edition of *The Merck Index*, which is of the same format as the preceding edition, is printed in clear type on English finish paper, bound in a dark blue Fabrikoid cover which is resistant to water, acid and mildew, and stamped in gold. The special prepublication price of the new book in the United States is $7.00 for the regular edition and $7.50 for the thumb-index edition; after publication, the price will be 50c higher for each of the aforementioned editions. The book will be sent prepaid when remittance accompanies reservation, and the book may be returned in 10 days for full credit if the recipient decides not to keep it.

Here, then, after a lapse of more than a decade, is the first opportunity to obtain a copy of one of the most useful, dependable, and reliable technical reference books ever published—*The Merck Index*— an Encyclopedia of Chemicals and Drugs.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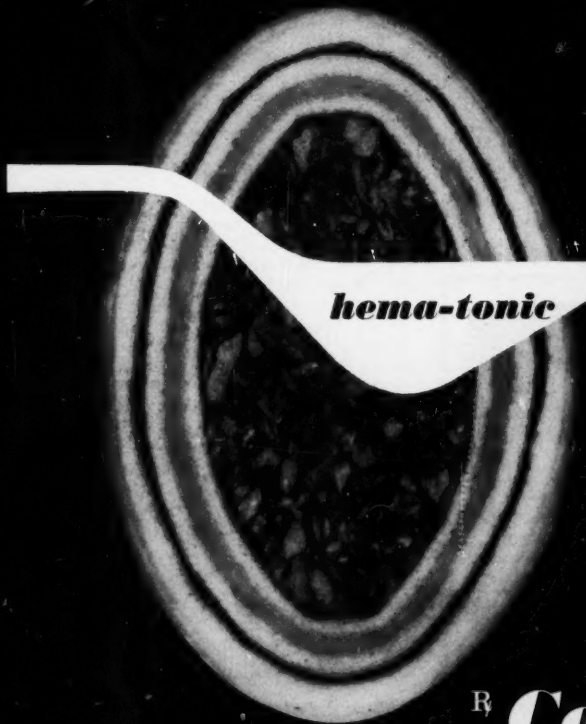

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MEDICAL RESEARCH

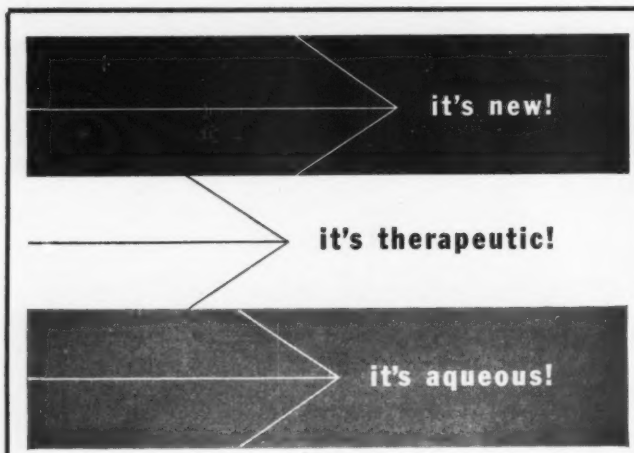
Dr. Max Sadove, Head of the Department of Anesthesiology at the University of Illinois, was elected organizing president of the Walter Reed Society at the first official meeting of the group held in Los Angeles at the close of the American Medical Association meetings.

The society which is sponsored by the National Society for Medical Research is comprised of those who have served as "human guinea pigs" in medical research or experimentation under the direction of a qualified scientist. It is named in honor of Dr. Walter Reed who risked his life in the fight against Yellow Fever and who first dramatized the use of the human volunteer in experimental medicine.

Dr. Sadove has frequently been a "guinea pig" and has just recently conducted some dramatic experiments with 50 volunteers at the University of Illinois. These experiments had to do with artificial respiration studies conducted at the request of the Defense Department. As a result of these experiments, the method of artificial respiration proved to be the most satisfactory from every standpoint has been officially adopted by the Red Cross and all military units.

Dr. Sadove is a native of Baltimore and received his medical training at the University of Maryland.

Other officers elected at the meeting were: Dr. Clinton H. Thienes, Head of the Department of Pharmacology & Toxicology, University of Southern California (Vice President); Dr. Lloyd L. Seager, Head, Department of Physiology & Pharmacology, University of Arkansas (Vice President); Dr. John P. McGovern, Chief, Out Patient Department, Children's Hospital, Washington, D. C. (Vice President); Miss Betty Jenney, Research Associate, University of Illinois (Secretary-Treasurer).



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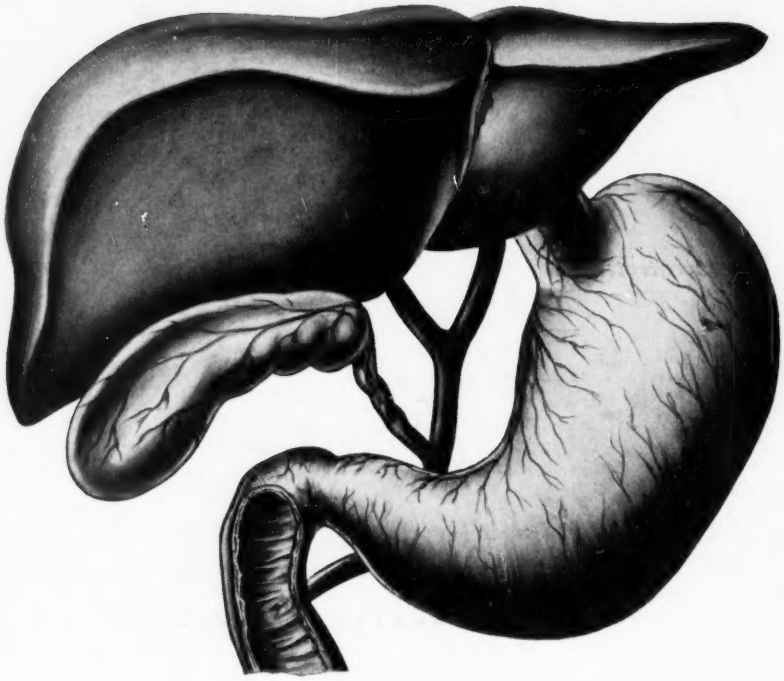

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